Report from the international workshop on schistosomiasis and reproductive health

22-25 January 2008, Lusaka, Zambia

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Report from the international workshop on Schistosomiasis and Reproductive Health 22-25 January 2008 Lusaka Zambia

Organised by:
The Zambia Bilharzia Control Programme
The Schistosomiasis Research Programme (SRP) at DBL-Centre for Health Research and Development, Denmark
The Research Network for Schistosomiasis in Africa
Centre for Imported and Tropical Diseases, Department of Infectious Diseases, Ullevål University Hospital, Norway
Department of Infectious Diseases, Skejby Hospital, Denmark

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Acknowledgement

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Organisers

The workshop was organized by The Zambia Bilharzia Control Programme, The Schistosomiasis Research Programme (SRP) at DBL - Centre for Health Research and Development, Denmark, the Research Network for Schistosomiasis in Africa (RNSA), Centre for Imported and Tropical Diseases, Department of Infectious Diseases, Ullevål University Hospital, Norway and Department of Infectious Diseases, Skejby Hospital, Denmark.

Opening session

Introduction

Thirty-six researchers and national coordinators and programme managers of schistosomiasis and HIV/STD control programmes from west, east and southern Africa, Europe and USA gathered at the Taj Pamodzi Hotel in Lusaka, Zambia, to discuss the impact of genital schistosomiasis on public health and its implications for national programmes for the control of schistosomiasis, HIV/AIDS and sexually transmitted diseases.

Background

Research in the field of genital schistosomiasis has given rise to the hypotheses that there might be a relationship between genital schistosomiasis and transmission of HIV, female infertility and morbidity.

Research has shown that women suffering from genital schistosomiasis have genital sandy patches and contact bleeding. There are several case reports discussing the possible causative association between genital schistosomiasis and cervical dysplasia and/or human papillomavirus. Furthermore, there is a recent study indicating that genital schistosomiasis may be refractory to treatment in adults.

Conducting research in genital schistosomiasis poses huge challenges. One major challenge is the difficulties in diagnosing genital schistosomiasis. The commonly used diagnostic tools such as urine filtration and faecal Kato-Katz have been proven to be insufficient in diagnosing genital schistosomiasis. The ova are located in highly focal clusters and may be missed in a biopsy, especially with histological sectioning of a biopsy. Moreover, taking a biopsy for the diagnosis of genital *S. haematobium* infection remains an HIV transmission risk for the patient and her partner until the inflicted wound has healed, raising ethical concern. Wet smears and PAP smears make a contribution to the diagnosis but the sensitivity is low.

Objectives and form

The overall objective of the workshop was to bring together researchers, national coordinators and programme managers with a relevant background to identify and discuss the impact of genital schistosomiasis on public health and its implications for national control programmes for HIV and STD as well as to identify future research needs and priorities.

A number of speakers were requested to present their recent and ongoing research covering the topics listed below. Participants were then given the opportunity to discuss and make recommendations for control of genital schistosomiasis in existing control programmes for schistosomiasis, HIV and STDs.

Content and topics

The workshop addressed the following topics:

- genital schistosomiasis as a public health problem
  - the possible association with HIV
  - the possible association with other STDs (and possible indirect effect on cervical cancer)
  - the possible effect of genital schistosomiasis on fertility and sexual behaviour
- diagnosis of genital schistosomiasis
- challenges in doing research on genital schistosomiasis
  - research in adolescents and children
  - immunological aspects of the transmission of HIV in the presence of schistosome eggs
- treatment of genital schistosomiasis

Outdoor toys are handed over to Kamulanga Primary School

Visit to school health programme

Thursday afternoon all participants went to John Howard Township to visit the Kamulanga Primary School, funded by the Japanese government. The school had approximately 1300 students which all underwent the school programme on "Schistosomiasis, soil transmitted helminths and HIV/AIDS control". Nutrition and personal hygiene were one of the buss words in the school programme, which among others revealed committment from the students to keep the toilet facilities and school area clean as well as to care for their personal hygiene. The school grew vegetables and

fruit to support the nutrition of the students and made home visits to provide family members with the same knowledge as their children. Furthermore, there was great focus on information on schistosomiasis, STH and HIV/AIDS through role plays, songs, drama, etc. In appreciation of the visit, the workshop sponsored footballs, hand-net and basket balls, jumping ropes and basket nets to the school.

Opening session

The workshop was officially opened by the Honorable Minister of Health, Dr B. Chituwo, Ministry of Health, Zambia and Dr N. Oernbjerg, Director of DBL. Dr J. Mwanza from the Zambia Bilharzia Control Programme chaired the workshop trough the opening session. The Honorable Minister of Health said that 2 million have schistosomiasis in Zambia, most of whom are mothers and children. Research is important in the Zambian decision making processes, and hopefully the affected communities will notice that we have held this consultation.

Conclusions and recommendations

Schistosoma haematobium frequently causes lesions in the urogenital organs. Gross haematuria and dysuria are commonly reported urinary tract symptoms, whereas pelvic pain and vaginal discharge in women and ejaculation discomfort in men are observed in genital schistosomiasis.

Female genital schistosomiasis is associated with HIV infection. The underlying mechanism is thought to be the egg-induced friable genital mucosa making women susceptible during intercourse with an HIV positive partner. Moreover, in men with HIV and *S. haematobium* co-infections, the inflammatory responses to egg deposition in the prostate or the seminal vesicles have been hypothesized to cause increased viral shedding in semen and may increase the risk of transmitting HIV.

It is essential that treatment for schistosomiasis is provided to children in all endemic areas for schistosomiasis transmission to prevent the complications and repercussions of the disease. All opportunities for treatment should be provided including preventative chemotherapy through mass administration complemented by availability of praziquantel in health centres and STI clinics. Health care providers in schistosomiasis endemic areas should be further sensitized to the symptoms, risks, treatment, and prevention of schistosomiasis and to the link between schistosomiasis and HIV infection.

Research priorities in female (FGS) and male (MGS) genital schistosomiasis

Evidence suggests that FGS is associated with HIV infection, and a similar association has been hypnotized for MGS. However, to turn evidence of an association into proof, and to document causative relationships and involved mechanisms, require further and comprehensive studies. A full understanding of the association between genital schistosomiasis and HIV require further elucidation of various aspects related to genital schistosomiasis as such, including diagnosis, clinical features and morbidity, treatment regimens and disease perceptions.

The possible interaction between HIV and genital schistosomiasis is complex and other sexually transmitted diseases (STI), age- and sex-related differences in water contact patterns, and differences in socio-cultural factors and economic living conditions are significant confounders. This results in the need for large population based longitudinal studies with complicated study designs including multiple drug treatment regimens, pre- and post treatment analysis, and a thorough analysis of socio-cultural factors and economic living conditions. Introduction of a schistosomiasis component in ART (anti retroviral treatment) studies seems a natural way forward.

Research priorities are as follows:

Morbidity, diagnosis and treatment of genital schistosomiasis

- Documentation of FGS and MGS as courses of reproductive tract morbidity with a focus on high intensity infections
- Studies on the role of FGS and MGS in primary and secondary infertility
- Further exploitations of clinical findings and manifestations in FGS, including optimisation of methods to identify sandy patches and other pathological manifestations and standardisation of clinical registrations and questionnaires
- Further studies on clinical findings and manifestations in MGS
- People's perception of FGS and MGS in the light of STIs as a significant confounder with a focus on symptoms and clinical manifestations
- Development of a sensitive, specific and widely accepted "gold standard" diagnostic technique for FGS and MGS, including the use of PRC and Elisa-ECP techniques on vaginal lavage specimens and optimisation of sampling techniques
- Optimising treatment regimes in FGS to address the proposed irreversibility of morbidity in adults and assessment of the effect of treatment in girls and young adults with different drug dosages
- Effect of praziquantel treatment in HIV positive individuals and further studies on the effect of treatment on symptoms and lesions in both MGS and FGS
- An analysis of the possible relevance of cryotherapy in treatment of genital tract pathology in FGS
- Further elucidation of the proposed spermatogenic apoptosis in MGS and its potential effect on fertility and reproductive health in men

Association between genital schistosomiasis, HIV infection and other STIs

- Confirmative studies that FGS predisposes to HIV infection and other STIs
- Further documentation that MGS may constitute a risk factor for HIV transmission

Immunological and other laboratory based studies to reveal mechanisms involved in the association between genital schistosomiasis and HIV infection

- Analysis of the possible role of angiogenesis, neovascularisation and increased levels of HIV receptors in genital lesions, in schistosome egg granolomas and in peripheral blood for the increased susceptibility to HIV in FGS

- An analysis of the HIV viral load in semen to document whether MGS due to egg induced inflammation in the prostate and seminal vesicles constitutes a risk factor for HIV transmission

- Elucidation of the possible role of a shift in the Th1/Th2 balance in individuals carrying both genital schistosomiasis and HIV infections in the increased susceptibility to HIV infection

Health Systems Research

- An analysis of appropriateness, feasibility and cost-effectiveness of introducing praziquantel treatment in STI clinics and other reproductive health facilities and services with a focus on anti-STI regimens in young women

Summary of the discussions

Epidemic Aspects of Genital Schistosomiasis with Respect to HIV

Dr Alex Simwanza from the Zambian National Aids Council presented the HIV epidemic in Zambia which shows the same disproportion of affected females as compared to males (18% and 13%, respectively) as the rest of sub Saharan Africa. Several studies on HIV prevalence have shown an unexplained gender quotient disfavouring rural women. In rural areas the differences between men and women is larger than in urban areas, with up to 6.4 HIV positive women to every man. Women from rural areas also have an HIV prevalence peak at younger ages. Hence risk factors in rural and urban populations may be different. In rural areas the difference between the young men and women (15-24 years) is even larger. In young women the HIV prevalence may be up to 8 times higher than in young men. In Africa, women have been found to be at a higher risk of HIV per sexual intercourse with an HIV positive person than heterosexual men.

Dr Simwanza reported that the Northern Province of Zambia is the least affected (8%) whereas the copper belt and Lusaka have 20 and 22% in prevalence, respectively. Condom use is 38%, and 20% will still have sex with a non-partner. PMTCT (prevention of mother-to-child transmission) is very low, being 22% and 8%) respectively. Knowledge of the infection is as high as 98%, but ART coverage is only 46% (of those who need it). ART has been rolled out after these figures were calculated. Dr Simwanza showed an extensive organisation chart where youth and religious groups as well as the private sector and NGOs are working with the National Aids Council.

The Social Aspects of Female Genital Schistosomiasis

Dr Heba Ali presented an interdisciplinary study on genital schistosomiasis in Egypt. The study attempted to draw on the approach that places reproductive health in a social and cultural context, where reproductive health is viewed as 'the ability of women to live through the reproductive years and beyond with reproductive choice, dignity, and successful childbearing, and to be free of gynaecological disease and risk' (Kattab 1999).

The study area was a remote village in the El Faiyum Hamlet where many had protected water, but where washing was still done in the canals. Many women had been treated by the Ministry of Health in mass treatment campaigns with praziquantel. Through focus group discussions and interviews it was found that abortions had been experienced by 33%, neonatal mortality by 33%, still births by 8% and 5% were infertile. Reproductive health problems were not discussed in the population. Urinary schistosomiasis prevalence was 17% (21/122). Female genital schistosomiasis (FGS) was defined as having at least one schistosome egg in cervical biopsy or sandy patches in the vagina or in the cervix. FGS was found in 50% of the infected women. These had more contact bleeding, erosions, polyps/ papillomata and leukoplakia than women without FGS.

Dr Ali pointed out that the study was designed as a small-scale pilot study and had some limitations. A single quantitative urine examination for *Schistosoma haematobium* is not sufficient, especially since mass therapy campaigns had been administered prior to the study. It can thus be assumed that the observed prevalence of schistosomiasis was an underestimation of the true prevalence in the study population. FGS may also have been underestimated due to the fact that the biopsies were rather small (< 5mm) due to the fear of bleeding from the biopsy sites, and due to the fact that the gynaecologists were reluctant to take them from sites suspicious of pathology. In addition, for ethical reasons, biopsies were not taken from the vagina or vulva.

She concluded that more research is needed to explore the association between schistosomiasis and reproductive morbidity. Furthermore, health care workers need training in the methods of detection and diagnosing FGS. Qualitative research is needed in order to better understand people's perception about this disease entity. Increasing health awareness among the population should follow. Moreover, the development of sensitive, specific and widely acceptable diagnostic techniques is urgently needed for any future clinical and epidemiological research into FGS.

Discussion: The biopsies should be avoided, and other objective diagnostic procedures for genital schistosomiasis are needed. Dr. Ali was asked about the differential diagnosis and the other causes for reproductive tract morbidity and replied that a limited number of tests were done for STIs (sexually transmitted infections). She pointed out that the village was remote and they had not expected sexually transmitted diseases. However 8% were found to have syphilis so there could have been a potential for further exploration of the association between FGS and STIs.

Female Genital Schistosomiasis Clinical Findings and Manifestations

Dr. Kjetland presented clinical work done in rural Zimbabwe with Blair Research Institute. Gynaecological and laboratory investigations for *S. haematobium* and STIs were performed in 527 women between the age of 20 and 49. The aim of the study was to describe the prevalence of gynaecological *S. haematobium* infection (FGS) and to differentiate FGS from STIs. Homogenous yellow and/ or grainy sandy patches, the commonest type of pathology in the genital tract, were identified in 243 (46%) women. Grainy sandy patches were significantly associated with *S. haematobium* ova only. Genital *S. haematobium* ova presence was also significantly associated with homogenous yellow sandy patches, mucosal bleeding, and abnormal blood vessels. Ova presence was not associated with ulcers, papillomata, leukoplakia, polyps, or cell atypia. Urinary ova excretions decreased with age, however, genital schistosomal lesions were found at equal prevalence levels in all age groups. If lesions are touched with a spatula 'crepitations' may be heard as the spatula moves over the sandy areas.

In conclusion, genital schistosomiasis may cause sandy patches, mucosal fragility and bleeding, and is probably chronic after the age of 20 years. Most cases would be missed if only urinary analyses were done.

Dr B. Randrianasolo (Madagascar) started off by acknowledging Professor Feldmeier and others who had brought attention to FGS as a neglected tropical disease entity. Dr Randrianasolo presented results from a clinical study conducted in two villages in Madagascar; Sirama (*S. haematobium* high-endemic, >50%) and Mataipako (<20%, low-endemic). The two villages were comparable in other aspects. The study aimed to explore the symptoms and clinical manifestations in the lower genital tract of sexually transmitted diseases. According to the study design praziquantel treatment was delayed for one month whilst women were treated for STIs. Symptoms and disappearance of symptoms were recorded at baseline (before any treatment), 1 month (after treatment of STIs only) and at 6 months (after treatment with praziquantel).

In the high-endemic schistosomiasis village only people with urinary schistosomiasis were included (n=147) and in the low-endemic village only people where no *S. haematobium* eggs were detected in urine were included (n=106). At baseline neovascularisations and inflammatory lesions were found significantly more often in the schistosomiasis endemic village. There was however no difference in the prevalence of sandy patches among the 2 villages (6% vs. 2%). Surprisingly, in the *S. haematobium* endemic area, there was less tenderness upon bimanual palpation of the uterus (6% vs. 22%, $p<0.001$) and there was significantly less "rough aspect of the cervix surface" (11% vs. 21%, $p=0.03$). After treatment (n=115) there were minor decreases in sandy

patches: 6/157 (3.8%) vs. 1/64 (1.4%) and neovascularisation: 17/157 (10.8%) vs. 4/64 (6.3%). Dr Randrianasolo reported that sandy patches are difficult to visualise and may have been overlooked in the study. Contact bleeding had not been recorded.

In this comprehensive study, Dr Randrianasolo found that 50% of the women co-infected with STIs and schistosomiasis had no subjective complaints. Although there was no difference in occurrence of STIs in the 2 villages in the schistosomiasis endemic village women reported significantly more pelvic discomfort ($p< 0.001$), dysuria ($p<0.05$) and gross haematuria ($p<0.05$) in the highly endemic village. This difference between the 2 villages remained after all the STIs had been treated at the 1-month inspection.

There was no difference between the schistosomiasis endemic and non-endemic areas with respect to discharge, dyspareunia, vulval itch and postcoital bleeding. However, upon closer analysis looking at intensity of urinary schistosomiasis infection (less or more than 50 ova/10mL urine) dyspareunia was found more often in women with high-intensity infections ($p=0.07$).

Discussion: Symptoms may be difficult to differentiate from the sexually transmitted diseases (eg. dysuria in both cases). The genital examination is complicated in the rural setting and the lack of good light, magnification and stirrups may make it difficult to see the lesions. It is therefore important to look for less complicated ways of identifying sandy patches.

In Niger, 25% of the population is at risk of schistosomiasis. Dr Garba (Niger) and his group aimed to increase the knowledge about *S. haematobium* infection and its relationship with reproductive health in a community of women living in a hyper-endemic village. The study included randomly selected females who had lived more than 1 year in the village. Women were invited to participate, provided they were not menstruating, not virgins, and were a minimum of 2 months post partum. Women were interviewed, underwent a gynaecological speculum investigation, and urinary examinations. Direct and gram stained genital secretions were examined.

The study population constituted of 150 women of whom 80% were below the age of 36 years. Swimming (83%) and washing (58%) were the two main water contact activities; 32% of the population had urinary *S. haematobium* infection. Dysuria decreased with age as did history of haematuria. *S. haematobium* ova in urine was not associated with dysuria, lower pubic pain, pollakisuria, pelvic pain, menstrual disorders, leucorrhoea, vulval itch, vulval lesions (incl. polyps), history of abortion, labour complications, still birth, premature delivery, infertility, condylomatous tumours, vulval and vaginal inflammation, cervicitis, cervical polyps, or cervix bleeding. 'Tumefaction' of the cervix was significantly associated with urinary *S. haematobium.*

Discussion: The term tumefaction was discussed. Dr. Garba explained this as increased size – swelling – of the cervix, not necessarily associated with signs of cervicitis and Dr. Randrianasolo confirmed this. Dr Kjetland asked if this could be measured. Dr Kaseba, gynaecologist from Zambia said that cervices are of many different sizes. It was then suggested that clinical registrations and questionnaires in the different groups should be

standardised and sharpened so that the study results could be compared. This would also hold true for the sandy patches, the description of pain, the visual/colposcopic inspections, and palpatory findings. Furthermore, the association between symptoms and infection should be analysed for confounders.

Dr C. E. Ramarokoto (Madagascar) from the Pasteur Institut in Madagascar reported that transabdominal ultrasonography has previously revealed echogenic foci and masses in women from *S. haematobium* endemic areas. In a community based study in Northern Madagascar, systematic examination of the genital tract was done with intravaginal and transabdominal probes. Interestingly by ultrasonography, cervix, vagina, the tubes and ovaries were not different in the schistosomiasis endemic and non-endemic area. There was no difference in number of polyps, cysts, hyperechogenecity, hydrosalpinges or volumes of cervix or uterus. Evaluated by transvaginal ultrasound the female genitals did not change after praziquantel treatment in any of the two villages.

Female Genital Schistosomiasis and HIV Transmission

Blair Research, together with the University of Zimbabwe, Biomedical Research and Training Institute and University of Oslo conducted an extensive clinical and laboratory study in a population of rural women in Zimbabwe. Kjetland and co-authors found sandy patches in 46% of the women. The HIV prevalence was 29% and herpes simplex type- 2 (HSV-2) prevalence was 65%. Permanently resident women between the ages of 20 and 49 years who were sexually active, non-pregnant and non-menopausal were included in a cross-sectional study, with a one-year follow-up. HIV was found in 41% (29/ 70) of women with laboratory proven genital schistosomiasis as opposed to 26% HIV positive (96/375) in the schistosomal ova negative group. In multivariate analysis *S. haematobium* infection of the genital mucosa was significantly associated with HIV seropositivity (adjusted OR 2.9, 95%CI 1.11- 7.5, p=0.030). All 7 women who became HIV positive in the study period (seroincidence 3.1%) had signs of *S. haematobium* at baseline. In accordance with other studies HIV was significantly associated with HSV-2 (OR 3.0, 95%CI 1.7- 5.3, $p<0.001$), syphilis and human papillomavirus. The highest HIV prevalence (45%) was found in the 25-29 years age group. There is some supporting evidence that can be drawn from other studies, which have demonstrated a higher level of HIV receptors CCR5 and CXCR4 in peripheral blood in *S. mansoni* infected individuals and more HIV receptors in genital lesions than in healthy tissue nearby. Furthermore, the sociological studies indicate that city prostitutes are often from rural areas, and in rural areas the HIV prevalence may be 6 times higher in young women than in young men.

Discussion: With the presence of chronic lesions one may suggest that the risk of getting HIV should maybe have been even higher. Women with genital schistosomiasis were found to have an almost 3-fold risk of having HIV. Other factors such as lifetime partners, dyspareunia and demographic data should be explored in more details. It was asked whether genital schistosomiasis is a progression of urinary schistosomiasis. In the ensuing discussion it was thought that the urinary and genital tracts were probably affected simultaneously through the venous anastomoses around the pelvic organs.

Dr P. Jourdan (Norway) quoted reports that have found genital ulcer disease and cervicitis to recruit immunologically active cells. Immune activation may increase both the number of target cells in the area and the number of chemokine receptors on each cell. Mononuclear cells from people with schistosomiasis are more susceptible to HIV infection in vitro than cells from people without schistosomiasis. This phenomenon has not yet been explored in genital cells from persons with schistosomiasis. Clinically, genital schistosomiasis is associated with abnormal blood vessels and mucosal bleeding. Studies have postulated that products secreted by *S. mansoni* ova may promote angiogenesis, similar to what is observed during the development of malignant tumours. This has led to the hypothesis that abnormal cells, receptors and blood vessels in genital schistosomal infection facilitate HIV transmission. This could be explored by further examination of biopsies taken from the female genital tract in relation to studies on FGS and the results may shed more light on the basis of increased susceptibility to HIV infection among women with genital schistosomiasis.

Discussion: Dr. Vennervald suggested that the analyses could also be done in other types of biopsies, which are more readily available, such as biopsies from the urinary bladder from European patients with urinary schistosomiasis. These biopsies are often taken routinely if the patient presents with urinary lesions.

Treatment of Female Genital Schistosomiasis

Based on the current knowledge Dr. Kjetland set out to answer if treatment of female genital schistosomiasis belongs in an STI clinic. Syndromic management of the STIs, based on concepts of aetiology and local knowledge of the efficiency of therapy, are strategies in STI and HIV prevention. In the syndromic approach treat index person and partners are treated for bacterial discharge or genital ulcers. According to a number of reports this is controversial. Furthermore, diseases that are not treated such as herpes simplex will recur. This may create marital discord among couples and also distrust among people in the performance of the clinics. Moreover, unnecessary treatment is costly for already strained economies. However, where diagnostic tools and transport are scarce treatment is given based on proven effect on the clinical entity.

Dr. Kjetland presented two sets of results from the 20-49 year-old women, who participated in the study from Zimbabwe.

Briefly, treatment was provided at baseline (40mg/kg) and (60mg/kg) at 3 months. Multivariate analyses were run controlling for HIV status, age, timing of treatment (early to late in the transmission season) and the sexually transmitted diseases. Praziquantel did not have a significant effect on sandy patches, mucosal bleeding, or neovascularisation. Furthermore some women were seen after 2 and 5 years. Their genital lesions remained unchanged. Urinary schistosomiasis ova excretion, however, ceased.

Women in the same cohort were asked about treatment prior to the study. Frequency of mucosal bleeding and sandy patches was significantly lower in women who had received treatment below the age of 20, even after correcting for current regular water contact and age. The different drugs used against *S. haematobium* seemed to have

different effect on the presence of genital morbidity. Lucanthonen hydrochloride (used before 1973), metrifonate (used app 1974-1995) and lastly praziquantel had, in this order, decreasing 'protective effect' against genital schistosomal morbidity. However, when adjusting for patient age at treatment, no difference was seen. In conclusion, female genital lesions could possibly be prevented by early treatment. However, once established as chronic morbidity, there seem to be no demonstrable effect of treatment and the lesions remain unchanged.

Dr Randrianasolo reported from the Madagascan study where, as previously mentioned, praziquantel treatment was delayed for one month whilst women were treated for STIs. Symptoms were recorded at baseline (before any treatment), 1 month (after treatment of STIs only) and at 6 months (after treatment with praziquantel). Five months after treatment with praziquantel there was no longer difference in urinary *S. haematobium* (or STI) prevalences in the two villages. Furthermore, symptom levels were now the same in the two villages. Although many women had no symptoms Dr Randrianasolo suggested that genital *S. haematobium* infection and STIs may have two symptoms in common: dyspareunia (not significant) and dysuria (significant). She suggested that pelvic discomfort and gross haematuria were symptoms of genital schistosomiasis and that praziquantel should be added to the existing anti-STI regimen in young women (aged 15-24) living in schistosomiasis endemic areas.

Discussion: Although lesions did not change after treatment in the Zimbabwean women, the women from the schistosomiasis endemic village in Madagascar benefited from the praziquantel treatment with respect to some of the symptoms. CAA analyses had also been done and showed a significant reduction after treatment. Dr. Kjetland drew attention to the fact that the effect of praziquantel was the same in HIV positive and negative individuals, and also that urinary ova excretion had gone down satisfactorily. Dr. Sacko (Mali) suggested that treatment may work differently in the different populations and that schistosomiasis may manifest itself differently in different populations. Anti-schistosomal treatment must be considered in adult men from *S. haematobium* endemic areas, who attend the STI clinic or other clinical settings with uro-genital complaints. However, the efficacy of praziquantel treatment on lesions in the female genital tract must still be determined. In a clinical setting it may however be worthwhile to try praziquantel for unresolved genital complaints, especially if the patient is young or has only recently had her 'schistosomal waterbody debut'. More research is needed on the effect of other treatment regimens on symptoms and lesions in the young and adult females.

Male Genital Schistosomiasis Clinical Findings and Symptoms

Dr P. Leutscher presented data on uro-genital symptoms reported by men living in an area of Madagascar where *S. haematobium* and STIs co-exist. Urethral discharge was significantly more frequently reported in the STI positive men compared to the STI negative men. Urethral discharge and/or dysuria were reported with different frequencies according to the different microorganisms: *N. gonorrhoeae* (75%), *C. trachomatis* (40%), *M. genitalium* (20%) and *T. vaginalis* (25%). Half of the men tested positive for an STI or for *S. haematobium* were asymptomatic. Dysuria and painful ejaculation, in addition to gross haematuria, were associated to positive *S.*

haematobium infection status. In men with moderate to high intensity of infection (≥ 50 eggs/10 ml urine), gross haematuria and uro-genital discomfort were reported significantly more frequently than in men with low intensity of infection (1-49 eggs/10 ml urine).

Dr Leutscher also presented data on semen analysis in a cohort of 27 *S. haematobium* infected men. The mean apoptotic rate at baseline was 6.8%, which is abnormally high compared to reports from other cross-sectional studies. Fifteen (56%) individuals were detected with ova in semen. Apoptotic rate was significantly correlated to seminal ECP level. At follow-up, the prevalence and intensity of egg excretion in urine and in semen declined significantly in conjunction with a significant reduction in mean apoptotic rate to 3.3%. The study demonstrated that the spermatogenic cells in *S. haematobium* infected men undergo apoptosis, which seems responsive to anti-*Schistosoma* treatment. Egg induced inflammation in the seminal vesicles could be an underlying mechanism.

In a Malagasy study population Dr C. E. Ramarokoto investigated men by transrectal and transscrotal probes. In males, hyperechogenic and calcified lesions have been demonstrated in the prostate and in the seminal vesicles concomitant with seminal egg excretion in non-immune male individuals infected during temporary stay in endemic areas. Men in this schistosomiasis endemic area had significantly more prostate hyperechogenecity and calcifications, and the seminal vesicles were significantly larger. Epididyma and hydrocele were equally prevalent in the two populations. In the schistosomiasis endemic village seminal vesicle hyperechogenicity and size decreased after treatment. The same was the case with prostate hyperechogenicity whereas calcifications remained.

Discussion: Symptoms of genital schistosomiasis have not been included in the DALY calculations for schistosomiasis. Some have reported pain on ejaculation and erection and alleviation of this after treatment to the extend that wives have come to ask for treatment for their husbands. In the light of these findings the burden of disease should be recalculated.

Male Genital Schistosomiasis and HIV Transmission

Dr Leutscher reported the findings from a study investigating the seminal inflammatory response to egg-infestation of the urogenital organs in 240 ejaculate donating men aged 15 to 49 years living in a *Schistosoma haematobium* endemic area of Madagascar. In 29 (12%) subjects detected with ≥5 ova excretion in the ejaculate, leucocytospermia, seminal lymphocytes and eosinophil leucocytes, were each significantly more prevalent compared that in 74 (31%) *S. haematobium* negative subjects ($p<.01$). In addition, seminal levels of interleukin IL-4, IL-6, IL-10 and tumor necrosis factor were significantly higher among seminal egg excreting subjects than among negative subjects ($p<.001$). Sexually transmitted infections did not act as confounders for the observed associations. At six months follow-up after systematic anti-schistosomiasis and STI syndrome treatment at baseline, the prevalence of seminal leucocytes decreased significantly amongst the previously seminal egg positive subjects. The same tendency was observed for the post-treatment levels of cytokines. Numerous studies have already shown an association between STI associated genital inflammation and HIV

propagation. Therefore, this study suggests that male urogenital schistosomiasis may constitute a risk factor for HIV transmission due to the egg-induced inflammation in the semen-producing pelvic organs.

Discussion: Epidemiological and clinical studies are needed to investigate into the hypothesized relationship between male genital schistosomiasis and increased risk of HIV transmission. A pilot study is currently taking place in Malawi by Dr. Risa Hoffman from UCLA University as principal investigator aiming to measure HIV viral load in semen from *S. haematobium* and HIV co-infected men before and after treatment.

Genital Schistosomiasis and Infertility

Dr A. Keita (Mali) presented a case of secondary infertility in a patient with urinary schistosomiasis from an irrigation area in Mali. The woman was found to have bladder calcifications. Hysterosalpingography revealed bilateral obstructions of the Fallopian tubes. Dr Keita suggested that community based research should be done on the association between urinary schistosomiasis and infertility and bladder cancer. He also suggested that the association between genital schistosomiasis and lymphatic filariasis should be explored as well.

Discussion: Dr Kjetland pointed out that there are many reports of concomitant findings of female infertility and genital schistosomiasis. *S. haematobium* is rarely found in the uterus. There are a few case reports of stunting and late pubertal development confirmed in animal models with decreased fertility and arrested development of corpora lutea. This may indicate that there may be hormonal disturbances in women with schistosomiasis. Furthermore, there are many case reports on tubal schistosomiasis and ectopic pregnancies. The Zimbabwean study did not find a higher rate of abortions or complicated pregnancies in women with genital schistosomiasis, but was not designed to detect the effect of *S. haematobium* on these fairly rare phenomena. Some case reports suggest that anti-schistosomal treatment has resulted in pregnancy. However, all previous analyses lack information about other diseases that may cause tubal obstruction. Although the Zimbabwean study has found some association with secondary infertility no study has yet been large enough to control for STIs. It would be very natural to assume that if *S. haematobium* causes secondary infertility it would also cause increased prevalence of primary infertility and sub-fecundity. Furthermore, the effect of *S. haematobium* infection on male infertility has not been explored. Male *S. haematobium* caused infertility could be a confounder in the analyses of effect of *S. haematobium* on female fertility.

Diagnosis of Genital Schistosomiasis

The clinical diagnosis of female genital schistosomiasis is currently dependent on a good light source or even a colposcope. The crushed biopsy of genital tissue is still considered the gold standard for the parasitological diagnosis of genital *S. haematobium* infection. However, the ova are located in highly focal clusters and one may miss them, especially with histological sectioning of a biopsy. Moreover, women in parts of the schistosomiasis and HIV endemic areas might neither have a choice of whether to have

intercourse or not nor the courage to suggest use of a barrier contraceptive method. Hence, taking a biopsy for the diagnosis of genital *S. haematobium* remains an HIV transmission risk for the patient and her partner until the inflicted wound has healed, and biopsies are thus not acceptable in these settings and are raising ethical concern. Wet smears and PAP smears may contribute to the diagnosis but the sensitivity is low.

University of Leiden has developed PCR in faeces and/or urine for a number of intestinal parasites and for urinary schistosomiasis. Robert ten Hove presented a brief list of possibilities for PCR analysis on faecal samples before he presented an example of using PCR as a tool for diagnosing schistosomiasis. The Assay 1 Real time PCR targets the *S. mansoni* (label FAM), *S. haematobium* (NED-MGB) cytochrome c oxidase subunit 1 and Assay 2 targets the schistosoma genus (label FAM) on rDNA repeat ITS2. Assays have been run on specimens from Northern Senegal consisting of 176 ethanol suspended stool samples stored at room temperature, There was a significant correlation between *S. mansoni* Kato Katz findings and PCR, i.e. the median PCR value was significantly correlated with egg count (Kappa 0.44, $p<0.01$). In a few urine samples from Gabon decreasing PCR values were observed with increasing intensity of infection. This was particularly obvious for specimens that had been stored at minus 80 C. Furthermore, stool samples stored at room temperature in ethanol seemed to provide a good correlation with the presence of urinary *S. haematobium*. The PCR analyses are expensive, but could hypothetically replace rural gynaecological investigation. In the field the samples for analysis could be obtained in a much simpler way. Furthermore, a single sample could potentially be used to diagnose all the STIs in a multiplex PRC approach.

Discussion: This test could probably be used on vaginal lavage specimens as well as on male genital specimens. Concerning specimens from male genitals the risk of contamination with urine and thereby eggs in urine was emphasised. For the same reason, it was stressed that in females it is important that the specimen is taken ‘deep enough’.

Urinary Schistosomiasis and HIV

Dr P. Ndhlovu reported on a multidisciplinary study conducted in rural Zimbabwe where 722 women registered for the study, 557 fulfilled the inclusion criteria and HIV status was determined in 544. Geometric mean egg count in those who had urinary schistosomiasis was 5.1 eggs/10ml urine. *S. haematobium* prevalence was highest in the youngest age (60%) group and declined to 29% in older individuals ($p<0.001$). Intensity of infection followed the same pattern. HIV prevalence was 20% in those below the age of 20 and peaked in the 25-29 year olds (44.4%) after which it declined to 17.1% in those above the age of 45. Women from the Shona tribe with urinary schistosomiasis had significantly more HIV than those without schistosomiasis ($p=0.02$). Women above the age of 35 years and infected with urinary schistosomiasis were more than twice as likely to be HIV positive than those who were urinary schistosomiasis negative.

The granulomatous inflammatory response induced by trapped schistosome eggs is responsible for manifestations of schistosomiasis. The major effector mechanism is an antibody-dependent cell-mediated cytotoxic reaction where CD4 positive cells are

active. The Th2 cytokine responses dominate in schistosomal infection while an optimal resistance to HIV is a predominantly Th1 response. Furthermore it has been hypothesized that the cells constituting the *Schistosoma* egg granuloma may contain specific receptors for HIV. Helminth infections in general suppress IL-2 and it has been hypothesized that this may increase the susceptibility to HIV transmission and propagation.

Dr Ndhlovu suggested that treatment and control of schistosomiasis may be an important complementary method to control the HIV pandemic in rural African populations. Future studies should include more than one method of schistosomiasis diagnosis, information about the time of HIV seroconversion and CD4 cell counts. Furthermore, differences in water contact patterns may confound the analysis of the association between HIV and schistosomiasis. Dr Ndhlovu suggested that further research is needed to explore new treatment strategies that will target the genital lesions in adults.

Discussion: The differences among the tribes were discussed. Dr Ndhlovu emphasised that a number of factors were not explored in this study and the lack of association between urinary schistosomiasis and HIV among the other tribes could be due to differences in duration of exposure to schistosomiasis.

Urinary and Genital Schistosomiasis Relations

Dr Kjetland reported that among women with urinary schistosomiasis in the different studies up to 65% also have schistosomiasis in the genitals and based on this one may ask if it is really necessary to do gynaecological investigations. In the Zimbabwean female genital study the mean intensity of urinary schistosomiasis infection was significantly higher in women with genital schistosomiasis ($p=0.05$). However 41% of the women without ova in urine had genital schistosomiasis. Furthermore, in the Zimbabwean study 123 of the 234 cases of genital schistosomiasis (53%) would not have been identified as *Schistosoma* egg positive without the genital inspection.

Schistosomiasis in HIV Positives

Dr V. Mwanakasale presented results from a study conducted among individuals aged 10-55 year in the copper belt of Zambia. They had found that the prevalence of heavy infections were lower in individuals with HIV and likewise, the proportion of haematuria. They only included people who had no signs or symptoms of HIV, and CD4 counts and viral load determinations were not done. Dr. Mwanakasale suggested that urine samples may be false negative for *S. haematobium* in HIV endemic areas and that a more sensitive technique for diagnosis is needed.

Discussion: It was asked if haematuria was quantified and compared in HIV positive and negative, but this information was not available. Similar to all the other genital schistosomiasis studies there was little information on the sociodemographic status. It was thus argued that HIV positive individuals may be from another segment of the population than HIV negatives. In the ensuing discussion it was contested that better

diagnostic methods are needed as other studies have found ample schistosomiasis in the HIV positive.

Dr P. Kallestrup presented the MUSH-study, also from rural Zimbabwe. The study aimed to compare the intensity of schistosomiasis infections in HIV negative, HIV positive, and HIV immunodeficient individuals. Furthermore, the efficacy of praziquantel in immunocompromised HIV positive individuals was determined and the study sought to explore the effect of treatment on the course of HIV infection in HIV and schistosomiasis co-infected individuals.

Contrary to findings in Kenya and Zambia the Zimbabwean study revealed no difference of egg excretion in HIV positive and negative individuals. The egg excretion decreased satisfactorily after treatment but levels of the circulating schistosome antigen, CAA, declined to a lesser extend in HIV positive individuals. The study in Zimbabwe was considerably larger than the other studies from Kenya and Zambia, but the intensity of *S. haematobium* was lower.

CD4 counts were lower in HIV negative patients with *S. mansoni* than in those without *S. mansoni*. In this rural Zimbabwean study untreated schistosomiasis was associated with a minor increase in viral load, while treatment arrested this increase. This was contrary to a small study in Kenya and a larger study in Uganda showing increased viral loads among the individuals who were treated. However, there were some differences among the studies. The Zimbabwean study was a randomised controlled study in an area with primarily *S. haematobium* infections of relatively low intensity whereas the Uganda study was primarily *S. mansoni* with higher intensities

Discussion: The main messages from this study were that egg counts can be used to diagnose schistosomiasis in HIV positive individuals and that praziquantel treatment is efficient in HIV positive patients. Although this was a randomised study it would have been an advantage to know more about the individuals who dropped out of the study and to have information about TB, episodes of clinical malaria and sociodemographic data. Dr Kjetland commented that the reported effects on viral loads were clinically insignificant and had been assessed over very short periods. The current findings regarding the difference in viral load would be of no clinical significance or relevance. Dr Kallestrup confirmed that HIV experts had stated this previously. Dr Kallestrup would like to see schistosomiasis research as a component in ART studies. Moreover, Dr Gundersen suggested that follow-up studies based on several of the presented studies would be interesting.

Future Prospects

Dr M. Chimbari pointed out that the pending climate change may affect schistosomiasis transmission. Even though Africa has contributed the least to these changes it is likely to be affected the worst. There will be varying precipitation as Southern Africa is likely to become hotter and drier whilst central Africa will become hotter and wetter. Furthermore, Dr Chimbari showed that the number of so-called extreme events (droughts, floods, cyclones) is higher in the developed countries but that the death tolls are highest in Africa.

The climate change may increase the temperature in higher altitudes, change human settlement patterns and affect the movement of people. It may also affect the number of vectors such as mosquitoes and snails by increasing the number of breeding sites. Between 1982 and 1996 the prevalence of *S. haematobium* increased in Matabeleland from 14.3 to 30% and *S. mansoni* was transmitted in areas where it had been absent in the 1982 survey. It has thus been hypothesized that malaria and schistosomiasis transmission will increase.

In order to intervene, there should be monitoring, early warning, forecasting, public education, and support for infectious diseases control. This is particularly challenging in African countries that have poor infrastructure, no funds dedicated for emergencies, low literacy rates in some areas, poor surveillance systems, armed struggles and government disagreements. Dr Chimbari listed possible funding opportunities on the subject of climate change: Global Environmental Facility (GEF) Trust Fund; Special Climate Change Fund (SCCF); Least Developed Countries Fund (LDCF); Kyoto Protocol Climate Adaptation Fund; IDRC funded Climate Change Adaptation in Africa (CCAA); WaterNet; Water Research Fund for Southern Africa (WARFSA); African Technology Policy Systems (ATPS).

Dr L. Mubila (Afro-WHO) presented the WHO strategic objective to reduce morbidity of schistosomiasis by prevention and regular treatment. At present WHO recommends two indicators for schistosomal morbidity – namely gross haematuria and ultrasound detectable changes in affected organs. WHO recommends management of cases and regular treatment of school aged children and other high-risk groups. Women of child-bearing age have been defined as a high-risk group along with occupational groups such as fishermen. Intersectorial collaboration is recommended including education, water and sanitation, as well as ensuring that developmental activity that may cause further spread of parasitic diseases must be accompanied by preventive measures. Dr. Mubila suggested that management of genital schistosomiasis should be integrated in the preventive measures for school aged children, in STI management programmes and/or in HIV/AIDS information packages.

The Way Forward

Dr P. S. Mbabazi (WHO, Geneva) gave an overview of WHO priorities and presented some questions. Neglected tropical diseases are known to have low fatality rates but high morbidity, and they are signs of systemic and systematic disadvantage. To a large degree the neglected diseases affect rural and remote populations, cause social stigmatisation and low-cost, effective public health tools are available. Furthermore, there may be paucity of data and minimal development of new tools and treatment.

WHO is dependent on data flow from the village levels to national and regional levels and also to WHO. It is a programmatic priority to combat disease by implementation of preventive chemotherapy and to monitor and evaluate adverse events, drug coverage, and efficacy. Halted chemotherapy before the parasite has been eliminated may render drugs ineffective, and both treatment and vector control are recommended strategies.

Dr Mbabasi stated that there is scanty information on management of adolescent illness as well as of co-morbidity and co-infections (e.g. schistosomiasis and HIV). Dr Mbabasi presented some questions from WHO:

1. The HIV-schistosomiasis relationship should be quantified and characterised
2. Global, regional, national data: what are the prevalence rates and disease burden data for schistosomiasis in HIV positive individuals and pregnant women?
3. The impact of treatment given to pregnant women should be quantified. Are there any associated benefits?
4. Does preventive chemotherapy (PCT) prevent HIV transmission? Can we enhance protection of populations with PCT? (given a focused implementation of school-based programmes – largely not childbearing, not sexually active): what is the evidence to further PCT?
5. Are current activities interfacing with the WHO-HIV department? If so, how?
6. If any, what is the current interface with national programmes?
7. How would current HIV-schistosomiasis activities fit into existing systems?
8. WHO needs to know what research is planned, including operational research to obtain further evidence
9. For global advocacy: It is necessary to develop a clear, strong message

WHO is setting up a register for pregnant women treated with ACTs and anti-helminthic drugs. It is implemented in many African countries already. With expanded access to treatment there is an increasing need to assess risks associated with exposure to drugs both for mother and child.

Mr M. P. Mapingure asked the question of what is fuelling the HIV epidemic in different populations. For example why are young women more susceptible to infection than men? Or why is the Tanzanian epidemic not as severe as the Zimbabwean? Mr. Mapingure went on to list factors that may influence the HIV epidemic, such as STIs, number of sexual partners, male circumcision, male viral load, HIV background prevalence. There may be an association between genital schistosomiasis and HIV. This relationship will be affected by the duration of the lesion.

He went on to present examples of e.g. mother to child transmission. There is now mathematical software that has been fitted to data collected from many studies. Attributable fractions of new HIV cases due to HSV-2 (and other STIs) have been calculated for different time periods. Mr. Mapingure wished to explore the role of both schistosomiasis and STIs in the current and past incidence and prevalence of HIV incidence and prevalence and thereby try to find an explanation for the differences in HIV prevalence in Tanzania (6.9%) and in Zimbabwe (25.6%).

Prof M. Taylor presented a study planned to take place in KwaZulu-Natal. It is designed as a prospective study in schoolgirls treated yearly, as recommended by WHO, and with several cross-sectional gynaecological surveys in sexually active young adult women. The hypothesis is that early treatment may prevent both HIV transmission and chronic genital lesions and the study will provide data on the effect of praziquantel on genital lesions and on a potential protective effect on HIV transmission.

Discussion: It is important to collect information about prior treatment, especially among the controls.

ANNEX 1

Workshop
Schistosomiasis and Reproductive Health
22-25 January 2008, Lusaka, Zambia

Tuesday 22 January			
Time		**Speaker**	**Chair**
8.30 – 9.00	Registration		
9.00 – 10.00	Delegates and invited guests arrive and are seated Arrival of Guest of Honour – Hon Dr B. Chituwo, Minister of Health, Zambia National Anthem Welcome remarks and speech from DBL representative Permanent Secretary, Ministry of Health calls upon the Hon. Minister of Health Speech by the Hon. Minister of Health Close of Opening Ceremony	 Dr N. Oernbjerg, Director of DBL Dr S.K Miti Hon. Dr B. Chituwo	Dr J. Mwansa
10.00 – 10.30	**BREAK**		
FGS in an HIV era – an introduction			
10.30 – 10.50	Social aspects of genital schistosomiasis in women	No. 1 H.A. Farook	J. Mwansa & P. Kallestrup
11.00 – 11.20	The HIV epidemic in Zambia	No. 2 M. Muteteka	
11.30 – 11.50	Insights into modelling techniques for schistosomiasis and sexually transmitted infections	No. 3 M. P. Mapingure	
12.00 – 13.00	**LUNCH**		
Clinical aspects of genital schistosomiasis – findings from the field			
13.00 – 13.20	Clinical findings of female genital schistosomiasis after controlling for confounders. Is urinary schistosomiasis a useful indicator?	No. 4 E. F. Kjetland	
13.30 – 13.50	Male genital schistosomiasis: Symptoms and semen analysis	No. 5 P.D. Leutscher	
14.00 – 14.20	Clinical, parasitological and ultrasound study of female genital Schistosomiasis, due to *Schistosoma haematobium* infection in an endemic Nigerian village, in 2005.	No. 6 A. Garba	
15.00 – 15.30	**BREAK**		
15.30 – 15.50	Uro-genital schistosomiasis in rural Madagascar:	No. 7	

	Ultrasonographical findings	C.E. Ramarokoto	
16.00 – 16.30	Summary and general discussion	Chair	
19.00	**DINNER**		

Wednesday 23 January			
Time	**Topic**	**Speaker**	**Chair**
HIV transmission in schistosomiasis endemic areas			
9.00 – 9.20	Schistosomiasis and HIV in Zimbabwe – the MUSH study	No. 8 P. Kallestrup	A. Garba & R. ten Hove
9.30 – 9.50	Urinary schistosomiasis and HIV	No. 9 P.D. Ndhlovu	
10.00 – 10.30	**BREAK**		
10.30 – 10.50	Male genital schistosomiasis and HIV	No. 10 P.D. Leutscher	
11.00 – 11.20	Genital schistosomiasis association with HIV	No. 11 E.F. Kjetland	
11.30 – 11.50	Female genital schistosomiasis in Madagascar: Symptoms and pelvic examination	No. 12 B. Randrianasolo	
12.00 – 13.00	**LUNCH**		
13.00 – 13.20	Viral load in blood after treatment – repercussions for the HIV epidemic with genital schistosomiasis in mind	No. 8 P. Kallestrup	
13.30 –13.50	Diagnosing urinary and intestinal schistosomiasis in the HIV area, a review of the literature	No. 13 V. Mwanakasale	
14.00 – 14.20	The effect of *S. haematobium* ova on mucosal blood vessels and cells with special attention to susceptibility to HIV transmission. An immunohistochemical and histopathological study.	No. 14 P.M. Jourdan	
14.30 – 15.00	Summary and general discussion	Chair	
15.00 – 15.30	**BREAK**		
Treatment and control of genital schistosomiasis			
15.30 – 15.50	Treatment of genital schistosomiasis, does it belong in a STD clinic?	No. 20 E.F. Kjetland	N. Midzi & P. Leutscher
16.00 – 16.20	WHO preventive chemotherapy strategy for control of Schistosomiasis in integration with other neglected tropical diseases.	No. 21 L. Mubila	
16.30 – 16.40	General discussion on treatment and control of genital schistosomiasis	Chair	
19.00	**DINNER**		

Thursday 24 January			
Time	***Diagnosis of genital schistosomiasis***	**Speaker**	**Chair**
9.00 – 9.20	The clinical and bedside investigations – unfeasible, uncomfortable, imprecise, dangerous and futile?	No. 15 E.F. Kjetland	B. Randrianasolo & B. Vennervald
9.30 – 9.40	ECP in female genital schistosomiasis, a useful analysis in some cases?	No. 16 N. Midzi	
9.50 – 10.00	The relationship between IgA or neopterin in vaginal fluids, genital smears and urine. Implications for field use.	No. 17 T. Mduluza	
10.00 – 10.30	**BREAK**		
			B. Randrianasolo & B.Vennervald
10.30 – 10.50	PCR for schistosomiasis in faeces. The technical approach to doing the same in vaginal lavage or genital smears	No. 18 R. ten Hove	
11.00 – 11.20	Eosinophil cationic protein (ECP), soluble egg antigen (SEA), and circulating anodic antigen (CAA) in male genital schistosomiasis	No. 19 P.D. Leutscher	
11.30 – 12.00	Summary and general discussion	Chair	
12.00 – 13.00	**LUNCH**		

Excursion
Visit to Primary School (Kamulanga)
Schistosomiasis, Soil transmitted Helminths and HIV/AIDS control programme activities

Friday 25 January			
Time	**Topic**	**Speaker**	**Chair**
	Ongoing and upcoming research		
9.00 – 9.20	Schistosomiasis in young women and girls in KwaZulu Natal	No. 22 M. Taylor	R. Banda & P. Leutscher
9.20 – 9.40	Male genital schistosomiasis as risk factor of HIV transmission – a study from Malawi	No. 23 R. Hoffmann	
09.40 – 10.00	Climate changes and tropical diseases	No. 24 M. Chimbari	
10.00 – 10.20	WHO priorities and the work of setting up a register for pregnant women treated with ACTs and antihelminths	P. Mbabazi	
10.30 – 11.00	**BREAK**		
	Research Priorities		
11.00 – 11.20	Genital schistosomiasis diagnosis and treatment Gaps in knowledge and research priorities	Chair from the session on diagnosis of genital schistosomiasis	E.F. Kjetland & L. Mubila *(Peter to assist with taking notes)*
11.30 – 11.50	HIV and schistosomiasis Gaps in knowledge and research priorities	Chair from the session on HIV transmission in schistosomiasis endemic areas	
12.00 – 12.30	General discussion and comments	Chair	
12.30 – 13.00	***Closing ceremony***		
	LUNCH		

ANNEX 2

Workshop on

Schistosomiasis and Reproductive Health

Lusaka, Zambia 22-25 January 2008

Participants

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ANNEX 3
Abstracts

ABSTRACT No. 1

Social aspects of genital schistosomiasis in women

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Female Genital Schistosomiasis (FGS) is a disease entity characterized by considerable individual and public health hazards. It is detected by the presence of eggs of *S.haematobium* in the upper or lower reproductive tract of women. It has been reported to lead to a group of morbidity conditions such as infertility, complications of pregnancy such as stillbirth, abortion and miscarriages, menstrual disorders, problems related to sexual intercourse, unspecified complaints related to blood loss, chronic abdominal pain, in addition to social segregation and related psychological problems.
Despite this, it remains a neglected disease entity and no reliable data exists on its prevalence and the true extent of the morbidity it causes.

The study aimed to explore the occurrence of FGS in a small rural population. As well as estimate the extent of reproductive morbidity among the women studied. A small village was selected in Fayoum Governorate in Egypt. All eligible women were interviewed and underwent a clinical and gynecological examination had a cervical smear and biopsy taken, in addition, a routine urine examination and blood analysis was done.

FGS was discovered among 50% of the women in the study. In addition, a high prevalence of other reproductive tract morbidities such as reproductive tract infections (vaginitis, 40%, cervicitis 22% and pelvic inflammatory disease 9%) and genital prolapse (54%) were also discovered.

NOTES:

ABSTRACT No. 3

Insights into modeling techniques for schistosomiasis and sexually transmitted infections

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Sexually transmitted infections (STIs) have been found to be a risk factor for HIV transmission. Likewise genital schistosomiasis has been found to be associated with HIV in rural Zimbabwe. The mechanisms for HIV propagation across the genital epithelium in females are believed to be similar to that of STIs (breach of mucosal barrier, recruitment of immunoactive cells or upregulation of HIV receptors).

Schistosomiasis is transmitted through water contact from childhood, whereas the STIs are transmitted by the very same mechanisms as HIV. The populations at risk of STIs (sexual risk behaviour) and schistosomiasis (exposure to infested water) may be completely different, or overlap as found in Zimbabwe.

Mathematical modeling has provided new insights on rates of spread of infection, epidemic trends, and effects of treatment. The effect of decreasing prevalence or eradication of the schistosomiasis may be estimated by modeling provided the confounding factors are fed into the mathematical formulas. Sexually Transmitted Disease Simulation Model (STDSIM) is one such model that allows simultaneous and interactive simulation of up to sixteen different STIs.

Herpes simplex virus type 2 has been suggested to account for 8-31% of the HIV cases. The prevalence of HSV-2 is 20-65%. Likewise genital schistosomiasis prevalence is approximately 50% and may therefore account for a number of HIV cases in rural areas. The modeling process could be useful in determining whether mass/treatment for schistosomiasis should be implemented in countries affected by the two epidemics.

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ABSTRACT No. 4

Clinical Findings in Gemale Genital Schistosomiasis After Controlling for Confounders and Severity of Infection

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Up to 75% of women with urinary schistosomiasis have *Schistosoma haematobium* ova in the genitals. The study aimed to describe the prevalence of gynecological *S. haematobium* infection and to differentiate the disease from sexually transmitted infections (STIs). Gynecological and laboratory investigations for *S. haematobium* and STIs were performed in 527 women between the age of 20 and 49 in rural Zimbabwe. Genital homogenous yellow and/ or grainy *sandy patches,* the commonest type of genital pathology, were identified in 243 (46%) women. Grainy *sandy patches* were significantly associated with *S. haematobium* ova only. Genital *S. haematobium* ova was also significantly associated with homogenous yellow *sandy patches*, mucosal bleeding, and abnormal blood vessels. Ova presence was not a predictor for ulcers, papillomata, leukoplakia, polyps, or cell atypia. Mucosal *sandy patches* seem to be pathognomonic for *S. haematobium* infection in the female genitals. Coexistence of ova and other lesions may not be causal.

NOTES:

ABSTRACT No. 5

Male genital schistosomiasis: Symptoms and semen analysis

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Symptoms

Background. Urogenital schistosomiasis and sexually transmitted infections (STIs) co-exist in most *Schistosoma haematobium* endemic areas in Sub-Saharan Africa, which poses a diagnostic challenge for health care providers in the management of patients with urogenital complaints, particular in settings with lack of adequate laboratory service.

Methods. Urogenital symptoms were researched by use of a semi-structured questionnaire at baseline and successively in follow-up surveys after systematic STI and anti-schistosoma treatment as part of a community-based study of reproductive tract morbidity in 236 men aged 15 to 49 years living in a *S. haematobium* endemic area in northern Madagascar.

Results. *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Mycoplasma genitalium* and/or *Trichomonas vaginalis* were diagnosed in 17% of the *S. haematobium* infected men. Half of the men tested positive for an STI or for *S. haematobium* were asymptomatic. No symptoms were associated to STIs found in men. Gross hematuria, dysuria, and painful ejaculation were associated with *S. haematobium* infection.

Conclusions. The study confirms the common co-existence of STIs and urogenital schistosomiasis. The rationale for empiric anti-schistosoma treatment of younger adults in *S.haematobium* endemic areas, by the addition of a single dose of praziquantel to existing anti-STI regimens, is discussed.

Semen Analysis

Background: The seminal vesicles are as frequently as the bladder a site for egg-induced inflammation in *Schistosoma haematobium* infected men. Egg excretion in ejaculate has been found associated with increased seminal leukocyte count and cytokine levels. The objective of this study was to evaluate the effect of male genital schistosomiasis (MGS) on spermatozoa DNA fragmentation.

Methods: Semen samples from men aged 15 to 49 years with positive egg excretion in urine were examined by an immune-histochemical staining method for terminal 3'-OH prior to anti-schistosoma treatment and 5 months later. Seminal ova, spermatozoa, and leukocyte counts were performed, in addition to measurement of seminal eosinophil cationic protein (ECP) level.

Results: In the cohort of 27 *S. haematobium* infected men, the mean apoptotic rate at baseline was 6.8%. Fifteen (56%) individuals were detected with ova in semen. There were no cases of oligospermia (≤20 millions spermatozoa/mL) and azospermia. Pyospermia (> 1 mill. spermatozoa) was observed in 5 (17%) men. Apoptotic rate was significantly correlated to seminal ECP level. At follow-up, the prevalence and intensity of egg excretion in urine and in semen declined significantly in conjunction with a significant reduction in mean apoptotic rate to 3.3%.

Conclusion: The study demonstrated that the spermatogenic cells in *S.haematobium* infected men undergo apoptosis, which seems responsive to anti-schistosoma treatment. Egg induced inflammation in the seminal vesicles could be underlying mechanism. Further studies are needed to evaluate the consequences of *S.haematobium* infection on male fertility.

NOTES:

ABSTRACT No. 6

Clinical, parasitological and ultrasound study of female genital Schistosomiasis, due to *Schistosoma haematobium* infection in an endemic Nigerien village, in 2005.

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Schistosoma haematobium is a major endemic disease in Niger. However, the impact of the parasite on the gynecological tract is not well known. Our study aimed to increase the knowledge about *Schistosoma haematobium* infection and its relationship with reproductive health in a community of women in a hyper-endemic village of Niger.

This cross-sectional study took place in April 2005 in the village of Kaou located near a temporary pond in the northern Niger. The study population was women of child-bearing age, having lived in the village for at least one year, and who had given their consent to participate in the study. The study subjects were randomly selected after a census was done of the entire village. The study included an interview, a general clinical and gynecological examination, a visual examination of the urine, a urine examination using Hemastix® for evidence of microhematuria, a parasitological examination after filtration of 10 ml of urine for *S. haematobium* eggs, and two smear tests of genital secretion for direct examination and for Gram's method, a hemoglobin test using the Hemocue® machine, and a ultrasound examination using the WHO Niamey protocol.

In total, 120 women were included in the study. The age group of 15-25 years (45%) and 26-35 years (35%) were the most represented. The overall prevalence of infection of *S. haematobium* was 32.2%, macrohematuria was 10.4%, and microhematuria was 44.4%. Anemia prevalence was 68.4%, and was significantly higher in women infected with schistosomiasis ($p<0.05$).

The overall frequency of clinical urological symptoms was 66.7% for reported pain during urination, 25.8% for pollakiuria, and 55.8% for lower pubic area pain. All the symptoms were more frequently reported in women infected with schistosomiasis than in those not infected, but the difference was not statistically significant. Leucorrhoea, abdominal pain, pruritus vulvae, and dyspareunia were the most commonly reported gynecological complaints, with a frequency of 82.5%, 58.3%, 55% and 46.3% respectively. Overall, in 51.5% of the cases, the cervix had lesions. Infertility and delivery complications were reported by 24.2% and 17.5% of the subjects respectively, a history of abortions by 13.3% and premature delivery by 5.8% of the subjects. The evidence of *S.haematobium* eggs was negative in all the smear tests. In the vaginal secretions of the subjects we found bacillus with positive Gram coloration in 47.2%, leukocytes in 20.4%, cocci with positive Gram coloration in 12.9%, diplococcus in 10.2% and yeast in 5.6%.

The obstetrical and gynecological manifestations of schistosomiasis are very evident. The treatment with praziquantel in endemic zones will contribute to the reduction in the morbidity caused by schistosomiasis in the female genital tract.

Key words: Female genital schistosomiasis, *Schistosoma haematobium*, obstetrical-gynecological tract, women of childbearing age, Niger

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ABSTRACT No. 7

Pre- and Post-treatment ultrasonographical findings in the urogenital organs in Schistosoma haematobium infected women and men

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Background: Ultrasonography (US) has so far not been used systematically in studies of *Schistosoma haematobium* associated pathology in the reproductive organs, although the technique seems potentially useful.

Methods: US was applied in this community-based study to assess *Schistosoma haematobium* associated pathology the uro-genital organs in women and men. Individuals (105 women and 116 men) from the high-endemic Sirama village with positive egg excretion in urine were compared to non-infected individuals (100 women and 118 men) from the low-endemic Mataipako village with negative results for both parameters. In addition to examination of the urinary tract by transabdominal US, the female genitals were examined by transvaginal route, whereas the male genitals were examined by transrectal and transscrotal routes.

Results: Pathology of the urinary tract was significantly more prevalent at baseline among women and men in the high-endemic Sirama village than in the Mataipako village. There was no difference in the prevalence and nature of abnormalities in the female genital tract, including volumetric measurements, between the two study populations. Significant higher proportions of men in the Sirama village compared to the Mataipako village were detected with hyperechogenic and calcified lesions in the seminal vesicles and the prostate, whereas there was no difference with respect to the external genitals. The mean size (the production of length and width) of the seminal vesicles was significantly larger in the Sirama village. Six months after anti-schistosoma treatment, the prevalence of urinary tract abnormalities had declined significantly for women and men in the Sirama village. Abnormalities and volumetric measurements of the internal male genitals also declined significantly.

Conlusion: The study has provided new insight into uro-genital morbidity in *S.haematobium* infected men and women, but the clinical significance of these findings remain unclear.

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ABSTRACT No. 8

Schistosomiasis and HIV in Zimbabwe – the MUSH study

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The Mupfure Schistosomiasis and HIV (MUSH) study is the result of a collaborative research project between the National Institute of Health Research (former Blair Research Institute), Harare, Zimbabwe and Department of Infectious Diseases, Rigshospitalet, Copenhagen, Denmark.

Apart from hosting 85% of the worlds estimated 200 million people living with schistosomiasis, the Sub-Saharan region of Africa also has the highest prevalence as well as total numbers of HIV-1 infected individuals. Schistosomiasis may by interference with the course of the HIV infection have great influence on the health of a large number of HIV infected individuals. Thus this study focused on the possible interaction between schistosomiasis and HIV in co-infected individuals. The study had three main objectives: 1) To compare the intensity of schistosomiasis between HIV negative individuals and HIV infected patients and describe the relationship between schistosomiasis intensity and immunodeficiency among the HIV infected, 2) To determine whether treatment of schistosomiasis with praziquantel is effective in immune suppressed HIV infected individuals, 3) To determine whether treatment of schistosomiasis with praziquantel has effect on the course of the HIV infection in co-infected individuals, evaluated by surrogate markers of disease progression.

All data were collected through the same field study conducted from October 2001 to June 2003 in Mupfure and adjacent areas in Shamva District, Mashonaland Central Province in Zimbabwe. To our knowledge it is the largest study exploring interactions of schistosomiasis and HIV to date and the first to be designed as a randomised controlled trial, which led to the creation of the MUSH Cohort.
In a cross-sectional survey a total of 2281 adults residing in the study area were screened regarding schistosomiasis and HIV status and a full set of information including three urine samples, one stool sample and HIV status were obtained from 1545 individuals. Among the total study population 26.3% were HIV positive and 43.4% were infected with schistosomiasis. 379 individuals were subsequently enrolled into a prospective cohort to ensure complementary data including quantitative measures of intensity of schistosomiasis and HIV related immunodeficiency and in order to carry out the treatment intervention studies.

There was no difference in egg excretion between HIV positive and HIV negative individuals infected with *S. haematobium*, *S. mansoni* or both. Moderately to severe HIV induced immuno-deficiency did not impair egg excretion of *S. haematobium* or *S. mansoni* in HIV positive individuals co-infected with low intensity schistosomiasis. Treatment of schistosomiasis with praziquantel resulted in similar and satisfactory reductions in egg counts between HIV positive

and HIV negative individuals, but HIV positive individuals cleared significantly less CAA – a schistosome gut-associated antigen indicative of active infection. Praziquantel may thus be less capable of inducing eradication of adult schistosomes in the immuno-compromised host. Schistosomiasis was over a three-month follow-up period associated with an increase in HIV replication among co-infected and successful treatment of schistosomiasis arrested this increase in viral load. Treatment of schistosomiasis also increased CD4-counts irrespective of HIV status.

In conclusion our findings suggest that control of schistosomiasis will not only reduce the substantial morbidity directly associated with schistosomiasis, but may simultaneously moderate an otherwise accelerated progression of HIV infection in the co-infected individual. In the current attempts to rollout anti-retroviral therapy, appropriate attention should be given to simultaneous schistosomiasis control and special guidelines for treatment of schistosomiasis in HIV co-infected individuals may need to be developed.

Perspectives of the results of the MUSH study

The results of our study provide important new insight that may prove relevant to several aspects of the interaction of concurrent infections and HIV in general and the dynamics of schistosomiasis and HIV co-infection in particular.

Primarily it is of importance to bring concurrent infections into focus to ensure appropriate attention not only to the impact these may have on the progression of HIV disease but equally to how HIV induced immunodeficiency may alter the pathogenesis as well as the efficacy of established treatment strategies of these concomitant ailments. Furthermore is the scale and severity of the HIV pandemic in the developing world a direct threat to the very fabric of society and the health infrastructure specifically. The magnitude of the epidemic has in places overwhelmed and paralyzed the health institutions to a degree where the care for other otherwise manageable infections fails. Renewed emphasis on the possible combined benefit of treating concurrent infections and the possible development of more efficient treatment strategies may induce much needed optimism and enthusiasm among the patients and stakeholders in the health sector.

Regarding the actual findings of our study the prospects evidently focus on individuals with schistosomiasis and HIV co-infection and thus areas where schistosomiasis is endemic and HIV prevalence may be high as well. Contrary to prior reports our results indicate that moderately to severe HIV induced immunodeficiency does not impair egg excretion of *S. haematobium* or *S.mansoni* in HIV positive individuals co-infected with low intensity schistosomiasis. This implies that egg counts can still be trusted when diagnosing schistosomiasis also in a population with high prevalence of *S. haematobium* or *S.mansoni*. In contrast egg counts may be less trustworthy when it comes to monitoring of efficacy of praziquantel in the treatment of schistosomiasis in the HIV co-infected host. Our praziquantel treatment study revealed that although similar and satisfactory reductions in egg counts were obtained between HIV positive and HIV negative individuals, the HIV positive individuals cleared significantly less CAA than HIV negative following treatment with praziquantel. This could be an indication of surviving worms due to reduced efficacy of praziquantel in the immunocompromised host and raises the question if the conventional treatment regimen is adequate for HIV patients.

Finally and encouragingly our results indicate that it makes good sense to treat schistosomiasis also among the HIV infected. Not only does it reduce the health impact of the schistosomiasis infection alone but it also seems to arrest an otherwise accelerated HIV replication. If our results can be confirmed in new independent studies, this may have wide implications since many of the regions of the world that currently carry the brunt of the HIV pandemic are also prone to high occurrences of schistosomiasis and often particularly so in areas that are less developed and therefore may be difficult to reach with anti-retroviral treatment programs. Here initiatives to control schistosomiasis could prove beneficial in slowing down HIV progression. Additionally such initiatives could potentially delay the time for initiation of anti-retroviral therapy and thereby postpone and possibly reduce the need for anti-retroviral treatment. In the current worldwide quest to roll-out anti-retroviral treatment the advantage gained from treating candidates for anti-retroviral therapy for their concurrent schistosomiasis should not be missed. Although we acknowledge that ART currently is the only strategy that has the potential to offer durable benefits for HIV patients it is our hope that appropriate attention will be devoted to the impact of schistosomiasis as well as other potentially harmful ailments in the design of ART initiatives.

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ABSTRACT No. 9

The prevalence of urinary schistosomiasis and HIV in females living in a rural community of Zimbabwe: does age matter?

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Recto: Urinary schistosomiasis and HIV in females in Zimbabwe

A cross-sectional study was conducted on 544 women living in Mupfure rural area of Zimbabwe to determine whether infection with urinary schistosomiasis is associated with HIV infection. Schistosoma haematobium infection was examined in urine samples and HIV infection was determined in sera. The prevalence of S. haematobium infection was highest (60%) in women below 20 years of age and declined to 29% in the oldest age group ($P < 0.001$). Overall, women infected with urinary schistosomiasis had an HIV prevalence of 33.3%, whilst women without urinary schistosomiasis had an HIV prevalence of 25.6% ($P = 0.053$). Women above the age of 35 years and infected with urinary schistosomiasis had a significantly higher HIV prevalence (37.5%) than those without urinary schistosomiasis (16.8%; $P < 0.001$).

KEYWORDS Schistosoma haematobium, HIV, urinary schistosomiasis, age

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ABSTRACT No. 10

Male genital schistosomiasis and HIV

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Background: To provide indicative data validating the hypothesized association between male genital schistosomiasis and HIV transmission, a study was conducted amongst men living in an area where urogenital schistosomiasis and STIs co-exist.

Methods: This study investigated the seminal inflammatory response to egg-infestation of the urogenital organs in 240 ejaculate donating men aged 15 to 49 years living in a *Schistosoma haematobium* endemic area of Madagascar.

Results: In 29 (12%) subjects detected with ≥5 ova excretion in the ejaculate, leucocytospermia ($>10^6$ leucocytes/mL), seminal lymphocytes and eosinophil leucocytes, were each significantly more prevalent compared to 74 (31%) *S. haematobium* negative subjects ($P<.01$). In addition, seminal levels of interleukin (IL)-4, IL-6, IL-10, and tumor necrosis factor (TNF-α) were significantly higher amongst seminal egg excreting subjects compared to negative subjects ($P<.001$). Sexually transmitted infections (STIs) with *Neisseria gonorrhoeae, Chlamydia trachomatis, Mycoplasma genitalium* and/or *Trichomonas vaginalis* did not act as confounders for the observed associations. At six months follow-up after systematic anti-schistosomiasis and STI syndrome treatment at baseline, the prevalence of seminal leucocytes decreased significantly amongst the previously seminal egg positive subjects. The same tendency was observed for the post-treatment levels of cytokines.

Conclusion: Numerous studies have already shown an association between STI associated genital inflammation and HIV propagation. Therefore, this study suggests that male urogenital schistosomiasis may constitute a risk factor for HIV transmission due to the egg-induced inflammation in the semen-producing pelvic organs.

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ABSTRACT No. 7

Genital Schistosomiasis Association with HIV in Rural Zimbabwean Women

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In a rural Zimbabwean community where we had investigated 83% of the eligible community members and found S. haematobium related lesions in 46% of the women, HIV in 29% and herpes simplex type- 2 (HSV-2) in 65%. We wished to determine the association between female genital Schistosoma (S.) haematobium infection and human immunodeficiency virus (HIV). Women between the ages of 20 and 49 years who were sexually active, non-pregnant, non-menopausal, permanent residents (>3 years residency) were included in a cross-sectional study was done with a one-year follow-up. Gynecological and laboratory investigations were performed for S. haematobium and HIV. Sexually transmitted infections, demographic and urogenital history were analysed as confounders.
HIV was found in 41% (29/ 70) of women with laboratory proven genital schistosomiasis as opposed to 26% HIV positive (96/ 375) in the schistosomal ova negative group (OR 2.1; 95%CI 1.2- 3.5; p= 0.008). In multivariate analysis S. haematobium infection of the genital mucosa was significantly associated with HIV seropositivity (adjusted OR 2.9, 95%CI 1.11- 7.5, p=0.030). All 7 women who became HIV positive in the study period (seroincidence 3.1%) had signs of S. haematobium at baseline. In accordance with other studies HIV was significantly associated with HSV-2 (OR 3.0, 95%CI 1.7- 5.3, p<0.001), syphilis and human papillomavirus. The highest HIV prevalence (45%) was found in the 25-29 years age group. Women with genital schistosomiasis had an almost 3-fold risk of having HIV in this rural Zimbabwean community.

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ABSTRACT No. 12

Female genital schistosomiasis in Madagascar: Symptoms and Pelvic Exam

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Symptoms

Background. Urogenital schistosomiasis and sexually transmitted infections (STIs) co-exist in most *Schistosoma haematobium* endemic areas in Sub-Saharan Africa, which poses a diagnostic challenge for health care providers in the management of patients with urogenital complaints, particular in settings with lack of adequate laboratory service.

Methods. Urogenital symptoms were researched by use of a semi-structured questionnaire at baseline and successively in follow-up surveys after systematic STI and anti-schistosoma treatment as part of a community-based study of reproductive tract morbidity in 253 women aged 15 to 49 years living in a *S. haematobium* endemic area in northern Madagascar.

Results. Thirty five percent of the *S. haematobium* infected women were co-infected with *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Mycoplasma genitalium* and/or *Trichomonas vaginalis*. Half of the women tested positive for an STI or for *S. haematobium* were asymptomatic. Among the women, vaginal discharge and dysuria were associated with an STI. Gross hematuria, dysuria, and pelvic discomfort were associated with *S. haematobium* infection.

Conclusions. The study confirms the common co-existence of STIs and urogenital schistosomiasis. The rationale for empiric anti-schistosoma treatment of younger women in *S.haematobium* endemic areas, by the addition of a single dose of praziquantel to existing anti-STI regimens, is discussed.

Pelvic exam

Background: *Schistosoma haematobium* is endemic in most parts of African continent and represents a major public health problem. Although the urinary bladder is the primary target organ for the migrating worm pairs, the genitals in both women and men are also commonly affected. A cross-sectional study was conducted to assess abnormalities associated to *S. haematobium* infection in the female lower genital tract, and to evaluate effect of anti-schistosoma treatment.

Methods: Women aged 15 to 49 years old with positive egg excretion in urine living in a small cluster of villages in high-endemic Sirama sugarcane plantation were compared to women with

negative egg excretion in the low-endemic Mataipako village. Pelvic examination by use of colposcopy was carried out at baseline, at T 1 month (after systematic STI treatment) and T 6 months (after systematic anti-schistosoma treatment).

Results. 152 women in Sirama and 122 women in Mataipako were included at baseline. One third of the women in both settings were diagnosed with an STI (*Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Mycoplasma genitalium* and/or *Trichomonas vaginalis*). Except from vaginal discharge no other findings were associated to STI. Cervicitis by inspection and cervical inflammation by colposcopy were significantly more frequent in Mataipako, whereas punctation/mosaicism was significant more frequent in Sirama. Sandy patches were observed 3.8% of the women in Sirama versus in 1.6% in Mataipako.Erosion/ulceration and polyp/tumour were also infrequently observed in the two study sites.

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ABSTRACT No. 14

The effect of *S. haematobium* ova on mucosal blood vessels and cells with special attention to susceptibility to HIV transmission. An immunohistochemical and histopathological study.

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Genital *Schistosoma haematobium* could be an important co-factor in HIV transmission. Genital ulcer disease and cervicitis have been shown to recruit immunologically active cells. Immune activation may increase both the number of local target cells, as well as the density of chemokine receptors. *S. mansoni* is associated with increased expression of HIV co-receptors CCR5 and CXCR4 in peripheral blood CD4+ T cells and monocytes. Furthermore, in vitro mononuclear cells from humans with schistosomiasis are more susceptible to HIV infection, than are cells from humans without schistosomiasis. Moreover, eosinophils have been found to be susceptible to productive infection with HIV. The phenomena have not yet been explored in genital cells in persons with schistosomiasis. By clinical observation, genital schistosomiasis is associated with mucosal bleeding. It has been postulated that products secreted by *S. mansoni* ova may promote angiogenesis, comparable to what is seen during the development of malignant tumours. In a cross-sectional study an almost threefold HIV-prevalence has been found in women with genital schistosomiasis. We hypothesise that immunactivation and neovascularisation in genital schistosomal infection facilitate HIV transmission. In archive biopsies taken from the female genital tract we wish to explore biological factors which may influence the transmission of HIV in women with schistosomiasis, provided ethical permission is granted. We wish to (1) establish the presence of immune cells, and identify by polyclonal protein detection (2) HIV receptors and (3) neovascularisation. The results may shed light on the susceptibility of women who have genital schistosomiasis

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ABSTRACT No. 15

The Clinical And Bedside Investigations of Genital Schistosimiasis in Women: Unfeasible, Uncomfortable, Imprecise, Dangerous and Futile?

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The crushed bedside biopsy of the cervix is deemed to be the golden standard for the parasitological diagnosis of female genital *S. haematobium*. Biopsies however, are taken for histology, the ova are located in focal clusters and may be missed by histological cuts. Moreover, women in schistosomiasis and HIV endemic areas might neither have a choice of whether to have intercourse nor the courage to suggest use of a barrier contraceptive method. Hence, taking a biopsy remains an HIV transmission risk until the inflicted wound has healed, raising ethical concern.

Wet smears and PAP smears may make a contribution to the diagnosis but the sensitivity is low. Up to 41% of women in endemic areas may have involvement of the lower reproductive tract without schistosome ova in urine. Hence, urinary filtration or dipsticks are insensitive indicators for genital *S. haematobium*. Increased levels of eosinophil cationic protein, Neopterin or IgA in cervico-vaginal lavage have only limited value in the diagnosis of female genital schistosomiasis. The PCR diagnosis, new for the genital tract, will be discussed in another abstract.

The co-existence of ova with clinical entities such as the numerous STDs makes it difficult to single out a cause of a current lesion or discharge. *S. haematobium* ova is associated with sandy patches in the genital mucosa, abnormal blood vessels and concomitant contact bleeding, and the clinical appearance of genital schistosomiasis may be mistaken for malignancy. Furthermore ova have been found in conjunction with ulcers, papillomatous tumours, leukoplakia, and polyps. However, *S. haematobium* ova may be found in almost every organ of the body and there may sometimes be no inflammatory reaction. Hence, the coexistence of *S. haematobium* ova and lesions or discharge may not always be causal.

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ABSTRACT No. 16

Assessment Of Eosinophil Cationic Protein (ECP) As A Possible Diagnostic Marker For Female Genital Schistosomiasis Among Women Living In A Schistosoma Haematobium Endemic Area

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Eosinophil cationic protein (ECP) levels were measured in vaginal lavage extracts from 518 Zimbabwean reproductive women, age range 15-49years, to assess the potential use of ECP as a diagnostic marker for female genital schistosomiasis (FGS). One hundred and fifty women had confirmed FGS status. These included 77 cases, women who had ova in genital tissue, and 73 controls, women who had no ova in genital tissue. Participants were treated with praziquantel at baseline and were followed up at 3 and 15 months post treatment surveys. ECP levels were determined using the enzyme linked immunosorbent assay (ECP-ELISa). ECP levels from 18 Norwegian women were used to calculate the diagnostic values of the test. FGS was diagnosed from the study population using genital biopsy and smears. Women were also diagnosed for urinary schistosomiasis using the urine filtration technique. The prevalence of urinary schistosomiasis was 39% at baseline and this declined to 8% and 6% at 3 and 15 months post treatment surveys respectively. There was a higher mean ECP level in women with FGS, 889.3ng/ml compared to the endemic control group, p = 0.027 (95% CI: 227.3-490.9). Mean ECP levels declined at 3 months post treatment following treatment of infected individuals. There was no correlation between ECP levels and tissue ova density, and urine egg intensity. The sensitivity and specificity for the ECP-ELISA test were 35%, 80% respectively. Our results indicate that FGS causes an inflammatory immune response that increases ECP levels in genital fluid. Treatment of schistosomiasis results in regression of pathology and a decline in ECP levels. How ever other factors such as allergy and microbial infection could also be responsible for increased ECP levels in genital mucosa. These conditions will affect the validity of the test in diagnosis of FGS.

NOTES:

ABSTRACT No. 18

Multiplex real-time PCR for the diagnosis of female genital schistosomiasis.

[1]Robert-Jan ten Hove, Jaco J. Verweij, Eric Brienen, Lisette van Lieshou1t

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Real-time PCR for the detection of intestinal parasites in faecal samples is increasingly used in diagnostic laboratories [1] and also as a tool in epidemiological studies [2]. Recently a multiplex real-time PCR was described for the detection *Schistosoma* DNA in stool and urine [3]. Designed primers and probes for *Schistosoma mansoni* and *S. haematobium* were combined as a multiplex with primers and probe for the detection of an internal control. The multiplex real-time PCR essay showed 100% specificity and high sensitivity. Additionally, the outcome of the multiplex real-time PCR, defined by Cycle threshold-values, showed a significant correlation with quantitative microscopic examination of human stool and urine samples.
The *Schistosoma* real-time PCR is also assumed to be a valuable tool in the diagnosis of female genital schistosomiasis (FGS). FGS, caused by infection of the parasite *S. haematobium,* is considered to be a major health problem in sub-Saharan Africa. Epidemiological and clinical studies on FGS traditionally rely on the microscopic detection of parasite eggs in biopsies, wet smears and PAP smears of the cervix. However, sensitivity of these diagnostic tools proved to be insufficient for diagnosing FGS. Moreover, the risk of HIV transmission for the patient and her partner increases through the inflicted wound from the biopsy [4].
Already several sexually transmitted micro-organisms are diagnosed by PCR on DNA isolated from cervical washings. These analyses can easily be extended with real-time PCR for *Schistosoma haematobium,* by using the same isolated DNA samples. The quantitative outcome of the real-time PCR can provide a better prognosis of FGS and evaluate the success of a therapy.
Moreover, for case studies conducted in remote areas where cold chain is not available, collected PAP smears can be stored in 70 % alcohol at room temperature until transported to a laboratory with real-time PCR facilities. The simple sample collection procedure in combination with the high throughput potential of real-time PCR can provide a powerful diagnostic tool for epidemiological and clinical studies on FGS in remote areas.

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ABSTRACT No. 19

Eosinophil Cationic Protein (ECP), Soluble Egg Antigen (SEA), and Circulating Anodic Antigen (CAA) in Male Genital Schistosomiasis

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Background: Epidemiological and clinical data regarding genital schistosomiasis are sparse. This is, in part, due to a lack of validated markers for genital infection. Urine egg count, the traditional marker of urinary *S. haematobium* infection, may not necessarily be representative for infection of the genitals.

Methods: Circulating anodic antigen (CAA) in serum, in addition to eosinophil cationic protein (ECP) and soluble egg antigen (SEA) were investigated in urine and semen samples from *Schistosoma haematobium* infected men aged 15 to 49 years before and six months after praziquantel treatment.

Results: A mutual positive correlation was observed between CAA, urinary ECP and SEA and egg count, except in comparison ECP with CAA. Seminal egg count was positive in 32 (48%) of 67 men providing two semen samples. A marked variation in seminal egg excretion was observed. Mean geometric levels of ECP and SEA were significantly higher in egg positive semen samples than in negative samples. SEA level in semen correlated positively with seminal egg count. Parallel to a significant decrease in urinary and seminal egg excretion after treatment, levels of ECP and SEA in urine and in semen, plus CAA also declined significantly.

Conclusion: ECP and SEA in semen constitutes supplementary diagnostic markers of male urogenital schistosomiasis**Background:** Epidemiological and clinical data regarding genital schistosomiasis are sparse. This is, in part, due to a lack of validated markers for genital infection. Urine egg count, the traditional marker of urinary *S. haematobium* infection, may not necessarily be representative for infection of the genitals.

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ABSTRACT No. 20

Treatment of Genital Schistosomiasis, Does It Belong in an STD Clinic?

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Urinary schistosomiasis is known to be associated with lesions in the female genital organs, particularly with the presence of "sandy patches" in the lower genital tract. This study sought to determine the effect of treatment with praziquantel on gynecological schistosomiasis in residents of a *Schistosoma haematobium* endemic area. A cohort study was conducted among 20- 49 years old women in rural Zimbabwe. The shape and size of lesions were mapped pre-treatment, and 3 and 12 months following treatment. Ova of *S. haematobium* were looked for in cytology smears, wet mounts, biopsies, urine and stool. Specimens were collected for detection of sexually transmitted diseases and cancer.

At baseline almost half of the 527 women included in the study had sandy patches. Although urinary ova excretion decreased following treatment (OR, 10.3 95% CI 3.8- 27.8, $p<0.001$), praziquantel was not associated with a significant reduction in genital lesions or contact bleeding ($p=0.31$-0.94). Sandy patches remained strongly associated with contact bleeding and vessel abnormalities even after treatment. Findings were independent of HIV status. Such lesions, common, and apparently refractory to treatment for at least 12 months, may be an important risk factor for both the acquisition and transmission of the human immunodeficiency virus.

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ABSTRACT No. 21

Preventive Chemotherapy Strategy For Control Of Schistosomiasis In Integration With Other Neglected Tropical Diseases: WHO Perspective

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Schistosomiasis continues to contribute to the burden of neglected tropical diseases with about 200 million people affected world wide. Early infection may go unnoticed but cumulative and long-term infections result in pathology in some organs of the body causing unrinary tract fibrosis, hydronephrosis, liver enlargement and associated ascites and bladder cancer as very late stage complications. Progression to these conditions can be retarded if cumulation of infection is stopped. The aim of preventive chemotherapy is to avert the widespread morbidity that results from heavy and prolonged infection with helminths. Early and regular administration of recommended antihelminthic drugs reduces the occurence, extent, severity and long-term consequences of morbity, and also contributes to reduction in transmission of infection. Morbidity control therefore is the WHO recommended strategy for schistosomiasis control achieved by large scale and regular treatment with praziquantel of the high risks groups in communities. However it is important that mass drug administrations be combined with other tools/activities that help to sustain the effect of the drugs. In this respect other supporting interventions such as environmental measures need to be equally addressed.

Large scale treatment delivery interventions are a strategy used in other disease control programmes as well, some of which share the same target groups, notably soil transmitted helmithiasis, lymphatic filariasis, onchocerciasis and - to some extent - trachoma. In order to improve the efficiency and cost-effectiveness in the implementation of these programmes and synergy in their outcomes, coordination and collaboration is recommended during implementation of interventions where the diseases overlap, , therefore leading to streamlining in the implementation of activities and synergism in outcomes of activities. As a working definition "integration" is defined as the creation of linkages among existing programmes for the purpose of improving delivery of interventions within the existing health system using resources available to the programmes concerned. Ultimately, the goal of promoting integration is to improve the effectiveness of the health system and not creating parallel or alternative structures.

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ABSTRACT No. 22

Schistosomiasis in young women and girls in KwaZulu Natal, South Africa

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Backgound. S. haematobium eggs have been found in the uterine cervix, vagina and vulva, as well as the urinary tract, but women may have genital schistosomiasis without urinary findings. Genital schistosomiasis is associated with a three fold increase in HIV prevalence. **Aim**. To investigate genital schistosomiasis in young women and girls and the effectiveness of regular treatment with praziquantel in reducing HIV incidence. **Objectives**. 1) To investigate the clinical manifestations of genital schistosomiasis in young rural South African women after controlling for STDs. 2) To investigate clinical signs and symptoms in young girls predictive of acute genital schistosomiasis. 3) To investigate schistosomiasis antibodies and antigens predictive of adult genital schistosomiasis. 4) To investigate whether schistosomiasis increases the expression of HIV receptors CCR5 and CXCR4 in blood and genital cells. 5) To investigate whether genital schistosomiasis infection increases HIV viral load and genital shedding. 6) To investigate whether genital schistosomiasis increases HIV incidence. 7) To investigate whether early and repeated treatment with praziquantel will reduce the susceptibility to HIV resulting in decreased HIV receptor expression, genital viral load and HIV incidence. **Method**. a) A cross sectional study and b) a prospective case control study are planned in rural KwaZulu-Natal (Ugu and Ilembe Districts). a) 888 sexually active women 16- 20 years of age will be interviewed for urogenital symptoms, obstetric history, and current and past STDs and investigated for schistosomiasis, blood, and photocolposcopic examination, pap-smears and cervico-vaginal lavage will be undertaken. b) 1407 pre-pubertal girls 10-12y will be enrolled in the study, complete a questionnaire and will be followed up for schistosomiasis, interviewed and treated with praziquantel annually until 550 have become sexually active, when schistosomiasis and blood will be investigated and photocolposcopic examination, pap-smears and cervico-vaginal lavage will be undertaken. Ethical clearance for the study has been obtained and informed consent will be obtained.

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ABSTRACT No. 24

Impacts of Climate Change on Health

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The phenomenon of climate change at global and local levels is now internationally accepted and the following predictions have been made for Africa (IPCC TAR, 2001); i) global mean temperatures of between 1.5^{o}C and 6^{o}C may be reached by 2100, ii) temperatures in Africa may increase by 0.2 ^{o}C to more than 0.5 ^{o}C per decade and the semi-arid regions of the Sahara and central and South Africa will be the most affected, iii) sea levels may rise by 15-95 cm by 2100, iv) Southern Africa will become hotter and drier, while Central Africa will become hotter and wetter and v) the probability of having extreme weather events (droughts, floods, typhoons, etc) will increase. While the climatic changes documented in the IPCC TAR 2001 are not disputed, it is their immediate direct impacts that are questioned with the long and sustained impacts being a subject of debate as it is difficult to establish a causal relationship for the long term impacts. This paper describes some of the impacts that climate change has had and is likely to have on human health, particularly vector borne diseases; argues why developing countries or African countries, in particular, will be affected most by climate change; and describes the coping strategies in place and recommended for minimizing the impacts of climate change on human health. The paper concludes that i) the impacts of climate change on human health are complex and require a transdisciplinary approach in dealing with them, ii) that vector borne diseases are likely to be influenced much more by climate change, iii) that sound strategies for adapting to the impacts of climate change are well documented with little action on the ground, iv) that there are serious challenges that may frustrate the efforts to minimize impacts of climate but also many opportunities that could be exploited; and v) that there needs to be more than political will among governments if adaptation activities are to be sustained.

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ANNEX 4

Newspaper articles from Zambian newspapers published in connection with the workshop

Zambia Daily Mail

Wednesday, December 12, 20(

NEWS IN DEPTH

Bilharzia: Neglected tropical disease

According to a report by the World Health Organisation , more than 200 million people worldwide are infected with bilharzia of which 85 per cent are from sub-Saharan Africa. Twenty million people worldwide suffer severe consequences from the disease. NKOMBO KACHEMBA writes on what the Zambia Bilharzia Control Programme has done so far to combat the predicament.

SCHISTOSOMIASIS, commonly known as bilharzia remains one of Zambia's biggest health challenges especially that it is one of the least developed countries in the southern African region.

It is estimated that close to two million people in Zambia are infected with bilharzia and that the prevalence rate is as high as 90 per cent in some communities.

World Health Organisation reports that an estimated 500-600 million people worldwide are at risk of contracting bilharzia and that it is prevalent among children below the age of 14 years.

To combat bilharzia, the Zambian government through the Ministry of Health with the Ministry of Education and other co-operating partners formulated the Zambia Bilharzia Control Programme whose main aim was to treat approximately two million infected people.

In Zambia, bilharzia is prevalent in rural areas and affects the underprivileged living near large masses of water.

According to a report from ZBCP, most Zambians do not have access to clean water and sanitation, including proper medical care thus increasing the chances of one being infected.

In children, bilharzia can cause malnutrition and can also damage the liver, bladder and kidney of the infected person if treatment is not administered on time.

ZBCP also reports that heavy infestation with intestinal worms can also cause anaemia in children and pregnant mothers.

A recent study by the Ministry of Health suggests that bilharzia reduces the child's potential to perform well in class and other activities.

Simple techniques in rural areas are used to identify children infected with bilharzia. Children usually have protruding stomachs as a result of the growth in the size of the liver.

ZBCP director Dr. James Mwansa said the programme has so far spent about US $2 million on the treatment of bilharzia and intestinal worms, which are prevalent in Southern and Eastern provinces.

Dr Mwansa said in the first phase, they treated about 1.2 million people in the two provinces with bilharzia and intestinal worms.

He explained that children especially were more vulnerable to infections in that they swam in areas which were highly infectious.

He said urinary bilharzia (haematobium) was prevalent in schools in Itezhi-tezhi and Kalomo while bilharzia of the stool (mansoni) was found in small pockets in Siavonga, Sinazongwe and Itezhi-Tezhi.

In communities where the prevalent rate was less than 10 per cent, only those infected were treated but where it was more than 30 per cent, mass treatment was recommended for everyone.

A CHILD infected with bilharzia with a protruding stomach as a result of the growth in the size of the liver.

Dr Mwansa said bilharzia should be given first priority just like any other disease and that more funding should be allocated to the programme so that more people could be reached.

"Most of the people who are affected are poor and they can't speak for themselves. Some are in the remot parts of the country and this makes it very difficult to have access to medical treatment, hence the need to deliver health services to them.", he said.

He said the drugs used for treatment of bilharzia were very affordable and that treatment was administered to people living in highly infectious areas once in a year to reduce morbidity.

He said programmes aimed at mitigating bilharzia were very simple but difficult to implement. So far, they have managed to sensitise the communities and schools on the preventive measures to combat it.

The programme has also trained more front line workers, community health workers and teachers to help administer treatment in communities.

The programme has also highlighted the importance of improving water sanitation in the country to help mitigate the disease.

To eliminate heavy infection of bilharzia, a drug called praziquantel is administered to the victim. Re-infection can occur but regular treatment is recommended to prevent further complications.

ZBCP, which has been working in the remotest part of the country, aims at reducing the number of people infected with bilharzia to 50 per cent in the next five years.

WHO recommends Albendazole as a good strategy for the treatment of intestinal worms in children to reduce further complications.

To determine the dosage of any drug, the height of children is measured and several questions asked on their daily activities.

Before administering treatment, ZBCP has to distribute food to the children in that most households in rural areas are poverty - stricken.

The Ministry of Health recommends that all primary school going children be given treatment where blood in the urine is the common symptom.

Recently in Lusaka's Ng'ombe township, bilharzia was reported and medical personnel are still on the ground to try and establish how prevalent it is before they make any recommendations.

Medical scholars suggest killing the molluse (snail host) using molluscicide but this has been disputed in that it would disturb the eco-system.

Parasitic diseases such as Bilharzia have been referred to as the Neglected Tropical Diseases (NTD) because of the attention they lack at both local and international level.

They have remained low on countries' public health agendas and do not receive the same levels of attention with diseases such as HIV/AIDS, Tuberculosis and Malaria.

WHO recommended that efforts to achieve the Millennium Development Goals (MDGs) should prioritise on intensified control of NTDs in that this would help reduce poverty.

Bilharzia prevalent in rural Lusaka, Southern Province

By NKOMBO KACHEMBA

THE Zambia Bilharzia Control Programme (ZBCP) says it has recorded a higher percentage of bilharzia infections among primary school going children in rural areas of both Lusaka and Southern provinces.

ZBCP chairperson James Mwansa said yesterday that out of 5,000 pupils examined, the organisation recorded a 90 per cent bilharzia prevalence.

Dr Mwansa explained that about 84 schools were selected in the two provinces adding that Southern Province recorded the highest infection rates. He said Siavonga, Kalomo and Ithezi - thezi districts in Southern Province had more than 50 per cent rate in schools whose pupils were examined.

Dr Mwansa also disclosed that ZBCP would in the first phase treat about 600,000 children and before the end of 2007, attend to an estimated two million children infected with bilharzia.

He also said recent studies conducted by the Ministry of Education, showed that bilharzia had an impact on school children's performance in class adding that the pupils with the disease normally had difficulties in doing simple activities in class.

Dr Mwansa said bilharzia caused so many complication such as cancer of the bladder, liver failure and anaemia.

However, he was disappointed that people infected took a lot of time to report such cases to health centres, making it difficult to treat the disease.

The ZBCP chairperson attributed the major causes of bilharzia infection to lack of clean water and sanitation.

Dr Mwansa said ZBCP was doing everything possible to reduce the number of bilharzia cases and to sensitise the communities on what precautions to take to prevent the infections.

Women with bilharzia more prone to HIV - expert

By NKOMBO KACHEMBA

WOMEN who are infected with Bilharzia of the Genitals are three times at risk of being infected with HIV/AIDS, Medical researcher Eyrun Kjetland has said.

Dr Kjetland who is in Zambia to attend an international workshop on HIV/AIDS and Reproductive health, said Female Genital Schistosomiasis (FGS) was incurable in adults.

She said she had carried out studies in Zimbabwe where 527 women had the infection as a result of swimming in streams infested with snails.

"All the women who were examined tested positive for FGS and they all had contact with snail infested water," Dr Kjetland said.

She said the common symptoms of FGS were itching in the genital area, a yellowish smelly discharge and vaginal bleeding.

Dr Kjetland said despite other women suffering from FGS, they did not have any symptoms and did not experience any pain.

"Eggs from the host (snail) usually manifest in the cervix. This causes infertility in most women and currently there's no cure," she said.

Dr Kjetland said most women who tested positive for FGS had suffered from common bilharzia in their childhood. She said the secret of dealing with FSG was tackling bilharzia in children. It is impossisble to treat in adults.

"Most Doctors know little about this disease and currently there are no programmes to educate people on FGS," Dr Kjetland said.

And another medical researcher, Heba Ali said despite FGS being first diagnosed over 100 years ago, no reliable data exists regarding its prevalence in various regions.

Dr Heba who carried out a study on FGS in Egypt said it was "very difficult" to diagnose the disease because its nature was not fully understood.

''It is hard to diagnose because it is usually mistaken with Sexually Transmitted Diseases (STD)s by both the patient and health professionals," she said.

Dr Heba said 80 to 100 per cent of the female population in endemic areas were at risk of having genital lesions.

She said most women suffered in silence. They cannot tell their husbands for fear of getting divorced.

Dr Heba said out of the 126 women who were tested for FGS in Egypt, 31 per cent had the disease.

She said most women thought that men were at a higher risk of contracting FGS and were ignorant about the fact that it could actually cause infertility.

And Zambia Bilharzia Control Programme (ZBCP) director James Mwansa said no studies had been done in Zambia on FGS.

ANNEX 5

SPEECH BY THE HON. MINISTER OF HEALTH, BRIGADIER GENERAL Dr B. CHITUWO, MP.

ON THE OFFICIAL OPENING OF THE INTERNATIONAL WORKSHOP ON HIV, SCHISTOSOMIASIS AND REPRODUCTIVE HEALTH.

22nd January 2008

Directors from the Ministry of Health;
Officials from DBL- Center for Health Research and Development;
Representatives from the Research Network for Schistosomiasis in Africa,
The chairperson of the organising committee; distinguished scientists; colleagues and friends,
All scientists, distinguished ladies and gentlemen.
May I simply say all protocols observed.

It gives me a great pleasure on behalf of the Zambian Government to address you all at this historic event – the international workshop on "**Schistosomiasis and Reproductive Health".**

Distinguished guests, I am reliably informed that this morning and the next 3 days, this gathering will have presentations and discussions elucidating how far we are in the knowledge about genital schistosomiasis and the impact on reproductive health. The aim of the workshop is to identify the possible impact that genital schistosomiasis might have on public health and the implication for national programs for the control of schistosomiasis, HIV and sexually transmitted disease; a topic of great importance not only in Zambia but the whole of Africa. This should eventually help us to identify the research areas that need to be further addressed.

Distinguished guests, schistosomiasis can cause significant morbidity and yet it is preventable and treatable. In fact one of the most important diseases caused by helminths in Zambia is schistosomiasis which has continued to retard human development in our society through ailments like malnutrition, poor growth in children, anaemia, kidney failure, cancer of the urinary bladder and lesions in the male and female genital organs. The latter may have a devastating impact on the reproductive health of people and may be a risk factor for the spread of HIV infection. This as we all know can seriously destroy national economy through loss of man hours due to ill health not to mention human suffering, and as such the control of schistosomiasis becomes a priority.

I am pleased to see that the issues to be discussed at this workshop include clinical aspects of genital schistosomiasis, with presentation of important findings from various field studies; the possible impact of genital schistosomiasis on the spread of HIV infection and the problems related to the diagnosis of genital schistosomiasis. Schistosomiasis in the context of reproductive health is a complex issue and calls for a multi-disciplinary approach. I am therefore very pleased to know that this workshop includes not only clinicians and biomedical researches but also social scientists and colleagues directly involved in the implementation of schistosomiasis control programmes.
All of these issues, ladies and gentlemen, will, I am sure, stimulate debate and discussion amongst the scientists, professionals and specialists present at this conference.

Distinguished guests, you may wish to know that in Zambia, bilharzia affects more than 2 million people, most of them being the poorest and most disadvantages people. Bilharzia is prevalent countrywide and school children are the most commonly and heavily infected group. The disease is also common in fishing communities, irrigation workers, farmers, women and young girls.
To address the problem, the government, through Ministry of Health formed a Bilharzia Control Program in collaboration with the Ministry of Education, The University of Zambia, various cooperating partners such as the WHO, The Danish Bilharziasis Laboratory now DBL, the Schistosomiasis Control Initiative of the Imperial College of London and other line ministries, to name but a few.

My hope is that your discussions at this meeting will lead to suggestions as how to improve control strategies in existing control programs for schistosomiasis, HIV and STD's and thereby to a strengthening of the collaboration between scientist and control managers working in these fields. I trust that this workshop will be both memorable and useful.

Let me take this opportunity to thank the DBL-Center for Health Research and Development for giving the Zambia the opportunity to host this workshop. We are also grateful that DBL and the Schistosomiasis Control Initiative (SCI) have provided financial support for this important meeting.

In conclusion, let me take this opportunity to welcome all delegates to our country, especially if this is your first visit to Zambia. Welcome to Lusaka and we hope that you will find Zambia stimulating and exciting.
I hope you have pleasant stay in our country and I trust that you will take time from your busy schedule to visit some of our world-renowned tourist attractions.
I wish you all the best in your deliberations and I thank you all.

Sponsored and organized by

BILL & MELINDA GATES foundation

The Schistosomiasis Control Initiative
and

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Zambian Bilharzia and other parasites Control Programme